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CONCRETIONS IN A LACRIMAL CANALICULUS CAUSED BY ACTINOMYCES

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Concretions due to actinomyces may occur in the superior or in the inferior canaliculus.

If the inferior canaliculus is involved, the first symptom is epiphora. There may be a slight swelling in the region of the canaliculus and dilatation of the punctum lacrimale (fig. 1). In early stages, however, these signs may be absent or so slight that they may be easily overlooked and a diagnosis of stenosis of the lacrimal passages made. On syringing the tear sac, there is no interference with the passage of fluid to the nose. On pressure in the region of the canaliculus, a droplet of pus appears at the punctum. In later stages the swelling of the canaliculus is noted at first sight, the ectasia of the canaliculus being considerable (fig. 2).

If the superior canaliculus is affected, there are no early symptoms, since an obstruction of the superior canaliculus does not cause epiphora. In later stages the physician may make a diagnosis of chalazion (which does not occur in this region), atheroma or inflammation, or a tumor may be suspected. In a case in which tumor was thought to be present (fig. 3), pressure caused a drop of pus to appear at the superior lacrimal punctum (fig. 4). The canaliculus was slit open. It contained several clumps of soft yellowish material, which did not adhere to the wall (fig. 5).

In the first case I saw, in 1933, the organism was isolated and studied by Dr. Ruys, bacteriologist.[1] It proved rather difficult to obtain the pure culture, which is necessary for a correct differentiation between Leptothrix (simple filaments) and Actinomyces or Streptothrix (branches).

The following technic, which I used on the advice of Dr. Ruys in 2 other cases, is so simple and efficient that it enabled me to isolate the organism in the laboratory of the ophthalmic hospital.

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1. Ruys, A. C.: Concretions in a Lacrymal Canaliculus Caused by Actinomyces, Brit. J. Ophth. **19**:385, 1935.

Fig. 1.—Early involvement of the inferior canaliculus produced by Actinomyces. There are slight swelling of the canaliculus and dilatation of the punctum lacrimales.

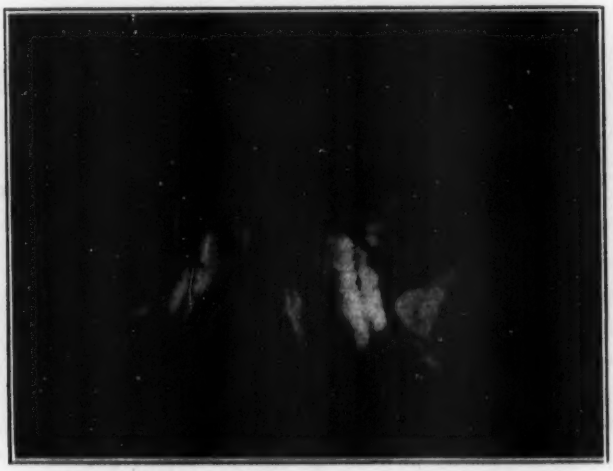

Fig. 2.—Later stage of the condition, showing considerable ectasia.

Fig. 3.—Involvement of the superior canaliculus. In this case the appearance caused the presence of a tumor to be suspected.

Fig. 4.—Appearance of pus at the superior lacrimal punctum on pressure in the region of the canaliculus.

Fig. 5.—Clumps of soft yellowish material found in the pus.

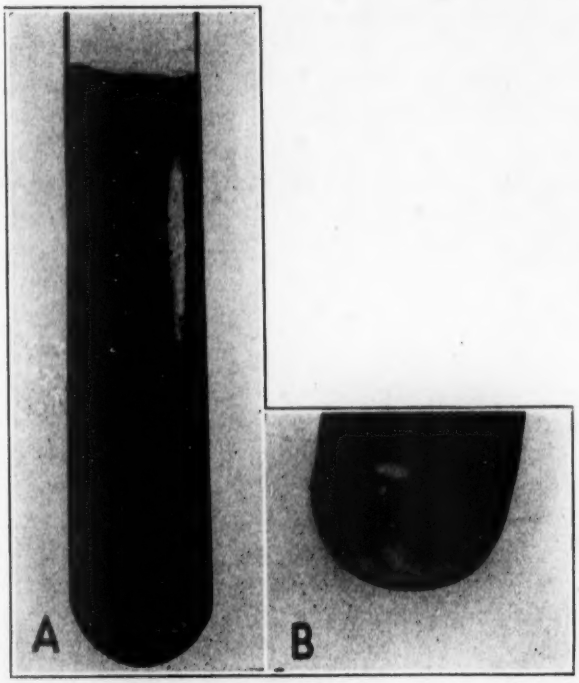

Fig. 6.—*A*, pure culture of Actinomyces grown in dextrose agar. *B*, a secondary culture grown in dextrose broth.

After the ducts were slit, a few concretions were isolated and a drop of 96 per cent alcohol put on each of them. After evaporation of the alcohol, which killed the bacteria, an emulsion was made of this material in sterile physiologic solution of sodium chloride. A test tube with sterile dextrose agar was put in a hot water bath until the medium became liquid. Then the temperature was allowed to drop again. Just before the agar became solid, a number of drops of the emulsion was added and the tube rolled between the hands in order to mix the material with the dextrose agar. The tubes were put in an incubator at 37 C. By this method it was easy to obtain a pure culture, which grew especially at a certain level under the surface of the dextrose agar (fig. 6 *A*). A secondary culture of material from this region grew in dextrose broth in the form of crumblike masses at the bottom, the fluid remaining perfectly clear (fig. 6 *B*). In some instances it was possible to get a pure culture without using alcohol simply by repeated washing of the concretion in physiologic solution of sodium chloride.

This method enables the ophthalmologist to obtain a pure culture. Further investigation of this interesting organism is possible only by a bacteriologist who has made a special study of the difficult field of Actinomyces.

SUMMARY

The clinical picture produced by Actinomyces in the superior and the inferior canaliculus is described, and a method is given for obtaining a pure culture of the organism.

TREATMENT OF OCULAR SYPHILIS

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Syphilis is a chronic infectious disease caused by Spirochaeta pallida, which invades all the tissues of the body. No organ is immune to the possible effects of the invasion. The manifestations of the disease may appear at any time as long as the micro-organism is active. It is the dermatologist who usually sees the first and most evident signs of the fresh infection and who is in a position to treat the disease possibly before the development of serious internal complications. The eye may be involved in the earliest stage of the infection. In ocular involvement vital and delicate tissues are affected.

Today the study of the eye is never neglected during the examination of the patient. Irregularity and "baying" of the pupil may be the first signs indicating possible syphilitic infection. Plastic iritis may occur in the early months of syphilis. Neuroretinitis may be observed early in the disease and may even disappear without treatment. It may, however, run an insidious course and remain dormant for years or appear as a late manifestation. Congenital interstitial keratitis is fairly common during the first few years of life and tends to resist treatment. The eyegrounds and the oculomotor apparatus demand frequent and repeated examinations in order to detect the possible presence of involvement of the nerve through basilar disturbance or pressure.

The ideal method of treatment calls for close cooperation between the ophthalmologist and the syphilologist. In the usual case the lesions of syphilis respond to regularly recognized methods of procedure, as, for instance, extragenital chancre of the conjunctiva, which would be treated in similar fashion to hunterian lesions elsewhere. Other manifestations, such as syphilids of the eyelids, gummatous infiltrations of the orbit, gummatous episcleritis and chorioretinitis, usually respond to the appropriate therapy employed for the early or late stages of the disease. As has already been indicated, in most cases there are no special procedures, ophthalmic or otherwise, to be adopted except in the presence of certain complicating features.

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AVAILABLE DRUGS

In order to prevent the serious ocular complications of syphilis, it is most imperative that the disease be recognized early and immediate treatment instituted. Continuous treatment should be given to prevent relapses, which are more apt to occur when treatment is interrupted with rest periods. The end results justify continuous treatment for years. The physician who administers the treatment must, however, be cognizant of the good and ill effects of the various remedies which he employs.

Arsphenamine still remains the most potent antisyphilitic drug. Mercurial preparations, at one time the standard remedy, are inferior to compounds of arsenic and of bismuth as a spirocheticide. Bismuth preparations and the newer arsenicals, while of great value, are still inferior to the arsphenamines. The average dose of asphenamine is 0.4 Gm. for men and 0.3 Gm. for women; the drug is administered intravenously, usually in courses of six to eight weekly injections, coincident with or alternating with courses of compounds of the heavy metals.

For a long time the ophthalmologist feared the action of the arsenicals because of toxic reactions from sodium arsanilate, which had produced amblyopia in numerous cases. Again, the development of atrophy of the optic nerve in cases of neurosyphilis in which tryparsamide therapy was employed also delayed the progress which had been made in the treatment of ocular syphilis with arsenicals. It is now known that tryparsamide when properly given as indicated is most valuable in the treatment of neurosyphilis and will rarely produce irritation of the optic nerve when contraindications are excluded. Although it has been shown that tryparsamide is without great spirocheticidal action generally, it has strong penetrating powers for the tissues of the central nervous system. It is of most value in the treatment of ocular syphilis associated with dementia paralytica of the tabetic form. The average dose is 1 to 3 Gm. administered every second week for at least twenty weeks.

Sulfarsphenamine is a sulfonate derivative of arsphenamine containing 20 per cent arsenic. It can be injected intramuscularly rather than intravenously. This advantage is outweighed by the high frequency of reactions it produces, and its use is now confined to children, who apparently tolerate it better than adults. The average dose is 0.6 Gm. for men and 0.4 Gm. for women. Silver arsphenamine is another arsphenamine compound; it contains 20 per cent arsenic and 13 per cent silver. It is considered by some syphilologists to be of value in the treatment of early visceral disease and neurosyphilis. The dose is approximately 0.2 to 0.3 Gm., and the drug is given intravenously.

Mapharsen, an arsenoxide, although less efficacious than arsphenamine, is a valuable drug in doses of 0.02 to 0.06 Gm. for those persons who are sensitive to the arsphenamines. Combinations of bismuth and arsenic, such as bismarsen, are being used with more frequency because the intramuscular route may be employed. Bismarsen contains 13 per cent arsenic and 23 per cent bismuth, and its action is slower than that of other arsphenamines. However, the results with bismarsen in the treatment of early syphilis are satisfactory if the injections are given at intervals of three to four days in doses of 0.1 to 0.2 Gm.

Acetarsone has shown good therapeutic action in some cases of neurosyphilis, but the high incidence of toxic reaction after its use, particularly nephritis, is a serious drawback.

Finally, it is emphasized that the use of iodides and their most beneficial effects should not be forgotten in the battle against syphilitic invasion. The average dose is approximately 5 to 10 Gm. daily.

Within the past few years the administration of large doses of arsphenamine by intravenous drip has been attempted. Hyman and his associates [1] have employed the gravity method of intravenous therapy and have administered as much as 1 Gm. of neoarsphenamine every fifteen hours in a 5 per cent dextrose solution. A total of about 5 Gm. is usually given. While this method yields immediate clinical and serologic results that are good, the toxicity, as manifested by the frequent occurrence of febrile reactions, toxicodermas, neuritides and fatal hemorrhagic encephalitis, places the method within the experimental stage. In addition, the possibility of reinfection is a drawback, as the immunity developed may not last for more than a few months or years. For the treatment of ocular syphilis the method of most value is still continuous therapy with bismuth compounds and arsphenamine.

Schereschewsky [2] advocated quinine for treatment-resistant syphilis, especially when the disease is associated with parenchymatous keratitis. He advised a dose of 2 Gm. daily for four days in addition to arsenotherapy. We have had no experience with quinine in this condition.

NONSPECIFIC THERAPY

Various methods of nonspecific antisyphilitic therapy may be employed to raise the body temperature to at least 104 degrees F. The fever may be produced by injections of malarial parasites, typhoid vaccine and sterile milk as well as by physical measures, such as hot

1. Hyman, H. T.; Chargin, L.; Leifer, W., and Rice, J. L.: Massive Dose Chemotherapy of Early Syphilis by the Intravenous Drip Method, J. A. M. A. **113**:1208 (Sept. 23) 1939.

2. Schereschewsky, J.: Therapieresistente Syphilis insbesondere die Keratitis parenchymatosa und ihre Behandlung mit Chinin, Klin. Wchnschr. **14**:381, 1935.

baths, electric blankets, heat cabinets, diathermy, electric induction coils and the inductotherm.

Nonspecific therapy plays an important role when the arsenicals and the heavy metals have failed. It has been shown that spirochetes in man are killed by a tissue temperature of 42 C. for one hour. Various hypotheses have been offered to explain the biologic reactions which occur when the fever is produced. Fever therapy apparently produces an immunologic response from the reticuloendothelial system.

It is believed that the high temperature tends to destroy the spirochetes and resorb the lymphocytic infiltrations of the lesions. It is also claimed that the reticuloendothelial system is stimulated to produce dereagins, which are carried to the inflammatory zone, where they attack and weaken the spirochetes. It is therefore of great value to keep the blood vessels patent by iodides administered orally in order to facilitate transportation of these reagins to the involved sites.

Hyperpyrexia will at times benefit atrophy of the optic nerve, keratitis, uveitis and pupillary lesions when specific therapy had previously failed. The response in cases of syphilitic interstitial keratitis is most noteworthy.

The ill effects of hyperpyrexia may be reduced by the preliminary administration of fluids, saline solution, dextrose and calcium. Patients with early involvement and minimal damage to the tissue receive the best results from treatment. Reenforcement by chemotherapy enhances the possibility of a good effect. The results from fever therapy are better when preceded by one or two courses of treatment with arsphenamine and a bismuth compound.

THERAPY OF SPECIFIC SYPHILITIC OCULAR LESIONS

Interstitial Keratitis.—This common lesion of congenital syphilis is resistant to treatment. Prophylactic therapy of early syphilis does not always prevent the later occurrence of interstitial keratitis. However, if prophylaxis can be extended to include the antisyphilitic treatment of the pregnant woman, the incidence of congenital syphilis, and accordingly of interstitial keratitis, would be markedly decreased. At one time it was believed that keratitis was a self-limited disease, and treatment was symptomatic. The modern trend, however, is definitely in the direction of active therapy. Carvill and Derby,[3] in a large and well studied group of cases described excellent results in 74 per cent of the cases in which treatment was given and in 38 per cent of the cases in which therapy was not administered, with a 3.6 per cent incidence of relapse in the former group as contrasted with 27 per cent in the latter group.

3. Carvill, M., and Derby, G. S.: Interstitial Keratitis, Boston M. & S. J. **193**:403, 1925.

Moore [4] advocated continuous therapy over a two year period consisting of alternating courses of arsphenamine and a bismuth compound. He claimed that most failures are due to underdosage. In some instances a Herxheimer reaction may be noted but is rarely of importance. Potassium iodide should be given simultaneously (3 to 7 Gm. daily) at the onset. Disappearance of the lesion proper may occur within twelve weeks, and further therapy may even lead to resolution of the usual residual corneal opacity. Schamberg and Wright [5] reported good results with alternate injections of a bismuth compound and sulfarsphenamine. Occasionally, cases will be encountered in which the disease is resistant to treatment, and a modification in therapy is advisable. The substitution of different arsenicals or bismuth preparations will frequently effect a cure in the cases in which the syphilis is recalcitrant. Beneficial results have been obtained by injection of foreign protein. Menagh [6] reported 4 cases of interstitial keratitis, in 3 of which the syphilis cleared after the addition of hyperpyrexia to chemotherapy. In 2 of these cases relapse occurred on several occasions prior to the institution of fever therapy.

Fever therapy tends to reduce the course of the disease and relieves the acute symptoms of pain, photophobia, blepharospasm and excessive lacrimation. Löwenstein [7] highly praised the value of roentgen rays, especially for patients with resistant corneal opacities. For those persons who respond poorly to intensive therapy, his method offers another weapon in the therapeutic armamentarium. Corneal transplantation is still another. Locally, atropine, ethylmorphine hydrochloride and hot compresses are useful early; in the retrogressive stage, yellow mercuric oxide is valuable.

Atrophy of the Optic Nerve.—The primary type of atrophy of the optic nerve observed in cases of cerebrospinal syphilis, tabes and dementia paralytica is fortunately not of frequent occurrence. If the condition is untreated, it leads to complete blindness. After blindness has occurred, obviously no replacement of the dead fibers can be accomplished. When the atrophic process is still unilateral and visual acuity and fields in the better eye are nearly normal, the condition may be aborted. When there is simultaneous bilateral loss of visual acuity and constriction of form and color fields, the prognosis is relatively bad.[4] There are two types

4. Moore, J. E.: Modern Treatment of Syphilis, Springfield, Ill., Charles C. Thomas, Publisher, 1933, p. 328.

5. Schamberg, J. F., and Wright, C. F.: The Treatment of Syphilis, New York, D. Appleton and Company, 1932.

6. Menagh, F. R.: The Treatment of Syphilis with Hyperpyrexia, Am. J. Syph. **21**:609, 1937.

7. Löwenstein, A.: Zur Pathogenese und Therapie der Keratitis parenchymatosa, Klin. Monatsbl. f. Augenh. **88**:306, 1932.

of treatment, the Swift-Ellis method of intraspinal arsphenamine therapy and hyperpyrexia. Intraspinal treatment is administered at intervals of two weeks in courses of seven to ten injections. It should be followed by a course of injections of bismuth compound and then repeated. Obviously, this is a very technical treatment, to be administered only by experts. The intracisternal route may also be employed to advantage. Combined subdural and intravenous therapy may lead to therapeutic shock, but the risk is far outweighed by the possibility of arresting inevitable blindness. Treatment should be continued for over six months after progression of the lesion has ceased.

The utilization of fever therapy is primarily reserved for those cases of atrophy of the optic nerve associated with paresis or dementia paralytica of the tabetic form.[4] Clark [8] reported an encouraging series of cases in which benefit was obtained in 8 of 12 cases after malarial therapy. Intramuscular injections of sulfur have also been used to produce high temperatures. Menagh [6] used hyperpyrexia in 10 cases of atrophy of the optic nerve. The disease in 3 was of long standing and showed no improvement. Four patients did well, 2 did poorly and 1 discontinued therapy. Menagh concluded that if there is damage due to a localized cellular infiltrate, as in tabes, the disease will respond to fever therapy and to early treatment. In dementia paralytica, on the other hand, the process usually spreads from the brain to the optic nerve and is then but part of a generalized and deep-seated infection with a poorer prognosis. In a similar vein, Culler and Simpson [9] stated that ocular syphilis due to exudative lesions should be expected to respond to fever therapy. Hargraves and Doan [10] demonstrated that artificially induced fever destroys lymphocytes. This decrease in perivascular infiltration of lymphocytes may account for part of the therapeutic effect, plus the direct thermolethal effect on the spirochetes. The results reported by 11 different observers for 98 patients with primary atrophy of the optic nerve treated by fever therapy showed 39 per cent improvement as contrasted with 54 per cent improvement obtained by Moore with subdural treatment.

Tryparsamide should be mentioned at this point because of its value in the treatment of neurosyphilis. It is to be used in the presence of atrophy of the optic nerve only when the patient has complete loss of vision.

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8. Clark, C. P.: Role of Malaria in Control of Atrophy of the Optic Nerve Due to Syphilis: Study of Twelve Cases, Arch. Ophth. **15**:250 (Feb.) 1936.

9. Culler, A. M., and Simpson, W. M.: Artificial Therapy in Cases of Ocular Syphilis, Arch. Ophth. **15**:624 (April) 1936.

10. Hargraves, M. M., and Doan, C. A.: The Physiological Response of the Hemopoietic Tissues to Artificially Induced Fever, in Abstracts of Papers of the Fifth Annual Fever Conference, Dayton, Ohio, 1935.

Lauber [11] advanced the theory that all of the drugs commonly used in the treatment of syphilis (arsphenamine, mercury and bismuth compounds and iodides) raise the systemic blood pressure and secondarily the retinal blood pressure. This, in his opinion, is the reason for the deleterious effects of antisyphilitic therapy in primary atrophy of the optic nerve. Therefore, he attempted to treat a series of patients by lowering the intraocular tension, since it was impossible to lower the systemic blood pressure. He treated 33 patients with a solution of a pilocarpine salt in 2 per cent or higher concentration, and if this was ineffective, he employed cyclodialysis. These two procedures led to a lowering of intraocular tension to a level of 10 to 14 mm. of mercury. In 27 of 33 patients, improvement was noticed. Unfortunately, the duration of the observation was not stated, and the results cannot be held as conclusive.

The Uveal Tract.—Involvement of the uveal tract and its component structures, notably, the iris, usually occurs in late secondary syphilis. Stokes [12] stated that 40 per cent of iritis is syphilitic and that iritis constitutes 73 per cent of the total ocular complications of early syphilis. It is commonly associated with a relapsing early syphilitic process. It is not the rule for iritis to occur as an isolated lesion but as a forerunner of more serious optic involvement, such as neuritis of the nerve or neuroretinitis. It is toward this complication as well as toward the iritis itself that therapy should be directed. The treatment should consist of alternating courses of arsphenamine and a bismuth compound with iodides by mouth. Therapy is continuous, as in early syphilis, with overlapping of the courses of arsphenamine. This is important, because a few days without treatment may be dangerous in the interim periods and may precipitate a relapse. It should be stressed that healing of the iritis is not an indication for cessation of treatment. Therapy must be continued for at least one year after the blood has given a negative serologic reaction, and the blood must be maintained persistently in this state. When iritis occurs as a feature of late syphilis, here again the stage of the disease is treated rather than the local manifestation. At this time, therapy should consist of at least two years of continuous treatment followed by at least two or more years of intermittent therapy. The drugs of choice are the arsphenamines and bismuth preparations. Cole and his associates [13] follow up this method with administration of compounds

11. Lauber, H.: Treatment of Atrophy of the Optic Nerve, Arch. Ophth. **16**: 555 (Oct.) 1936.

12. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1934.

13. Cole, H. N.; Moore, J. E.; O'Leary, P.; Stokes, J. H.; Wile, U. J.; Clark, T.; Parran, T., and Usilton, T. J.: The Clinical Outcome of the Treatment of Latent Syphilis, Ven. Dis. Inform. **13**:351 and 371, 1932.

of the heavy metals for as long as ten years after discovery of the syphilitic process. Bismuth preparations are undoubtedly of greater value than mercurials in these cases and are less toxic.

The local treatment of iritis resolves itself into the employment of atropine and its derivatives for the dilatation of the pupil with the intent of breaking any adhesions which may have formed between the lens and the iris. Rest in bed and the administration of salicylates for relief of pain round out the therapy. Gieske and Moore [14] reported good results in 87 per cent of cases of early syphilitic iritis and practically no residual damage in the iris in 58 per cent of cases of late syphilis. The occurrence of uveoparotitis in association with syphilis has been noted, and, according to Folger,[15] many forms of therapy have been tried, but none has proved of any real value.

Chorioretinitis.—This lesion may occur in congenital syphilis prior to the onset of interstitial keratitis but is more frequently a complication of acquired syphilis. The appearance of this lesion has been noted during treatment with a compound of one of the heavy metals other than arsphenamine, and in 1 case described by Zimmermann [16] six relapses were noted. As these lesions do not occur during arsenical therapy, longer courses of arsphenamine are advised with a suggested change from the arsenical first employed to a slightly different arsenic compound. Foreign protein therapy as well as hyperpyrexia may also be of benefit and may be utilized alone or in conjunction with chemotherapy. The chorioretinitis of congenital syphilis runs a comparatively mild course, and its treatment is that of the stage of the disease proper.

Dacryocystitis.—Involvement of the lacrimal sac may occur in about 2 per cent of the patients with congenital syphilis. The condition is usually unilateral, and the treatment is essentially surgical.

COMPLICATIONS OF AND REACTIONS TO THERAPY

Tryparsamide.—The utilization of this drug in cases of neurosyphilis has again contributed to the ophthalmologist's distrust of the arsenical group. Tryparsamide has a definite sphere of usefulness in the treatment of neurosyphilis but should not be employed when the optic nerve or retina is involved. Sloan and Woods [17] recently reviewed the literature and collected reports of 2,087 cases in which tryparsamide was administered. Six and three-tenths per cent of the patients had subjective

14. Moore, J. E., and Gieske, M.: Syphilitic Iritis, Am. J. Ophth. **14**:110, 1931.

15. Folger, H. P.: Uveoparotitis (Heerfordt): Report of a Case, Arch. Ophth. **15**:1098 (June) 1936.

16. Zimmermann, E. L.: Syphilitic Iridocyclitis with a Consideration of Factors Influencing Its Occurrence, Arch. Ophth. **53**:549, 1924.

17. Sloan, L. L., and Woods, A. C.: The Effect of Tryparsamide on the Eye, Am. J. Syph. **20**:583, 1936.

reactions and 3.5 per cent had objective complaints. They stated that there are two types of reaction. The first is the acute and less common type. It consists of the development of almost complete blindness within several days after the first few injections. The second type is decidedly more common and is chronic. It consists of contraction of the visual fields with retention of normal central vision and the absence of objective signs of atrophy of the optic nerve. They observed that in patients with normal optic nerves, fields and vision prior to tryparsamide therapy, there is little danger of any serious ocular damage if the administration of the drug is permanently discontinued at the first appearance of defects of visual fields. An occasional temporary, alarming but not serious untoward reaction is that of a nitritoid character appearing usually after several injections have been administered.

Arsphenamines.—That the arsphenamines are still the most potent antisyphilitic remedies at one's disposal is no longer a disputed subject. Their reputed toxic effects on the ocular apparatus have been disproved by the relative infrequency of reactions in thousands on thousands of cases. Zimmermann [18] has subdivided the toxic effects of the arsphenamines on the eye into three groups.

True Toxic Reactions: The only true toxic arsphenamine reaction involving the normal eye occurs during the nitritoid crisis. This general congestive reaction includes flushing of the face, swelling of the lips and eyelids, profuse perspiration, pallor, dyspnea, rapid pulse, vomiting, suffocation and even death. In addition, the eye exhibits hyperemia of the conjunctiva. This reaction may occur during or immediately after injection. The administration of the arsphenamine should be stopped immediately, and, if necessary, epinephrine administered. Other optic structures, especially the optic nerve, are never affected by arsphenamine. A secondary, but rare, toxic ocular complication occurring usually in the presence of an arsenical exfoliative dermatitis is superficial keratitis or corneal ulcer.[4]

The Jarisch-Herxheimer Reaction: This name is given to an efflorescence of the local syphilitic manifestations, which occurs after the first few injections of arsphenamine. It is usually a phenomenon of secondary syphilis, but it may complicate late syphilis. Zimmermann [18] expressed the belief that the Herxheimer reaction was of clinical importance only in patients with optic neuritis or primary atrophy of the optic nerve. He cited a case of his own and several others culled from the literature in which there occurred a violent hemorrhagic exacerbation of a preexisting optic neuritis with permanent visual damage after a single large dose of arsphenamine. He also has noted sudden complete loss of

18. Zimmermann, E. L.: The Role of the Arsphenamines in the Production of Ocular Lesions, Arch. Ophth. **57**:509, 1928.

vision in patients with primary atrophy of the optic nerve after the institution of arsenical therapy. He advised the administration of a heavy metal compound first to this type of patient or the use of very small doses of the arsenicals. Moore [4] stated that these reactions must be rare as he has never seen them. He expressed the opinion that he did not believe it necessary to employ long preparatory treatment with compounds of the heavy metals, especially cases of atrophy of the optic nerve. For optic neuritis, he advised starting treatment with small doses (i. e., 0.1 Gm. of arsphenamine) but increasing the dose rapidly at five day intervals to an average amount. Moore further observed that while the normal eye is unaffected, the diseased eye may be seriously injured by a Herxheimer reaction. This may appear either as an intensification of an already existing lesion, as a flare-up in a quiescent lesion or as the unexpected appearance of an inflammatory process in structures previously apparently uninvolved. According to Stokes,[12] one third of the practitioner's troubles comes from the nitritoid reaction.

Ocular Relapses: This effect is a result of insufficient arsphenamine therapy. The optic lesions may occur as part of a neurorecurrence or as isolated phenomena. The most common types are optic neuritis and iridorelapse. The probable mechanism is the destruction by insufficient arsenical therapy of all the spirochetes with the exception of those lurking in the depths of the eye or the far corners of the central nervous system. After an incubation period of several months exacerbations occur in these regions and rear their ugly heads as neurorecurrences. The only appropriate form of treatment is the immediate institution of intensive arsenical therapy. Dreyfus [19] recommended four to six courses of arsphenamine, each consisting of 8 to 10 Gm. of the drug. Treatment is continued until the tests of the blood and spinal fluid have become negative and have remained so for one year. Periods of rest from treatment are definitely not permitted.

Errors in Treatment.—Kazas [20] stated that there are five errors in the treatment of ocular syphilis. These are mentioned with a view to thoroughness, although complete agreement is not implied.

(*a*) Commencement of therapy with bismuth or arsphenamine instead of mercury may lead to biotropic reactions with undesirable complications.

(*b*) The provocative test for diagnosis may produce a temporary thriving of the spirochetes.

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19. Dreyfus, G. L.: Spezifische und unspezifische Tabestherapie, Deutsche Ztschr. f. Nervenh. **84**:14, 1925.

20. Kazas, I. I.: Five Errors in the Treatment of Syphilis of the Eye, Sovet. vestnik oftal. **7**:230, 1935.

(*c*) Insufficient dosage due to fear of toxicity of arsphenamine is a third error. A knowledge of the essential pharmacologic effects of arsphenamine, i. e., vagotonicity and acidophilia will avoid this.

(*d*) Monotherapy is a mistake.

(*e*) Inability to distinguish between insufficient dosage of arsphenamine and the effects due to overdosage is the final error.

Kazas treats his patients with injections of a soluble mercurial every day for the first two weeks. He then follows with arsphenamine, a bismuth compound and the iodides. His basic rule is the administration of as much arsphenamine as the patient can tolerate.

SURGICAL TREATMENT, ITS INDICATIONS AND CONTRAINDICATIONS

The influence of trauma in the development of sites of elective localization in syphilis is well known. The development of gummatous infiltrations in the healing scars of syphilitic wounds has been noted in many instances. The unfortunate features of this complication are its utter unpredictability and its usual occurrence in the one patient who should have been spared. It is easily understandable, therefore, that the ophthalmologist is hesitant in operating on a patient with syphilis, especially if it is in the active stage. Nevertheless, recent case studies have shown that the large majority of patients with syphilis may be operated on with impunity from the point of view of wound healing. However, those tissues which have already shown gummatous change should be left alone, as extensive and destructive results might ensue. When the indications point toward an operation, no time should be lost in advising it when it is deemed an emergency procedure. However, the postoperative course should include the institution of antisyphilitic therapy. Too frequently the operation is deferred until the ocular condition has advanced to the point at which the chances of arresting the process are slight. In cases in which therapy is not urgent, treatment of the systemic infection is indicated and may be followed at some future date by the necessary operative procedure.

SUMMARY AND CONCLUSIONS

Instead of presenting a statistical study of a group of cases of ocular syphilis in this paper, we have described our experiences in the treatment and observation of the disease. The accepted modern forms of treatment are indicated. The ideal antisyphilitic drug is arsphenamine or one of its congenitors. It should be given in conjunction with either mercury or bismuth compounds, in combined continuous courses over a period of years. Iodides should be used in all of the various stages and clinical phases of the disease. In the usual case of syphilis complicated by diplopia, disturbance of the ocular muscles, iritis or keratitis, especially

before degenerative changes have set in, the routine methods of antisyphilitic therapy are sufficient to prevent and cure the invasion of the optic structures. Herxheimer reactions are usually avoided if two or three preliminary injections of a mercury or a bismuth compound are given before the institution of arsphenamine. If a Herxheimer reaction develops, treatment should not be stopped if destruction of tissues is to be prevented. Neurorecurrences are usually the result of inadequate or short courses of intermittent treatment.

Arsphenamine and neoarsphenamine may be replaced by mapharsen, silver arsphenamine or sulfarsphenamine as already indicated. In cases in which there is no response to routine treatment, and especially when there are progressive changes, injections of tryparsamide together with the administration of bismuth compounds or iodides should be given for at least a year. Precautions should be taken against atrophy of the optic nerve.

The Swift-Ellis and the Swift-Ellis-Ogilvie method of intraspinal therapy should be tried in cases of resistant ocular syphilis associated with neurosyphilis. Such treatment will often reverse the spinal fluid reaction to normal and occasionally improve the clinical picture.

The other form of supplemental treatment, hyperpyrexia, produced by inoculation with malaria, injections of biologic products or mechanical means, may reverse the state of the spinal fluid in over 40 per cent of cases and arrest the clinical progress in about 15 per cent. The patients who receive the least beneficial response from therapy are those who have had neurosyphilis for more than ten years and present old lesions of a degenerative type plus severe involvement of the spinal fluid.[2] Reversals in the state of the blood and spinal fluid do not always indicate satisfactory clinical improvement.

The recent trends in the therapy of ocular syphilis offer a much more hopeful prognosis than is generally believed. The institution of the newer remedies together with those proved efficacious over a period of years will greatly lessen the incidence and prolongation of ocular complications.

2 East Fifty-Fourth Street.

IRITIS DUE TO BACTERIA AND BACTERIAL TOXINS ASSOCIATED WITH DENTAL SEPSIS

EXPERIMENTAL PRODUCTION IN LABORATORY ANIMALS BY ADMINISTRATION OF THESE TOXINS

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The relation between ocular diseases and oral sepsis has long been recognized. Articles [1] on ocular diseases caused by dental infection have appeared in the dental literature as far back as 1839 and serve to establish the recognized clinical association between diseases of the mouth and diseases of the eye. The medical literature is replete with experimental investigations concerning the production of iritis by the administration of various bacterial agents obtained from multiple body foci, through various routes of administration. Most of the experimental workers hopefully allied themselves in their research with the attractive theory of Rosenow [2] (1915), viz., that bacteria have a specific tendency to localize in certain tissues of the body, dependent on some peculiar inherent property, and based their studies on this concept. However, this present work is more especially concerned with the particular role of dental sepsis in the production of iritis experimentally.

The fact that many observers who have made contributions to this subject used methods that have not been uniform, obtained results at variance one with the other and drew widely different conclusions seems to suggest that the subject is surrounded by much that is as yet unknown. It seemed desirable, therefore, to throw some further light on the investigative work accomplished thus far by presenting a series of laboratory experiments on albino rabbits, in which I studied the effects of the bacteria and bacterial toxins found in the diseased processes of infected human teeth on the production of iritis in these animals.

In attempting to elucidate further the possible etiologic role of dental sepsis in the production of iritis, one must take cognizance of the many difficulties to be encountered in a work of this kind. The acute

From the Department of Ophthalmology, St. Louis University School of Medicine.

1. Black, A. D.: Ocular Diseases Resulting from Dental Lesions, Ophth. Rec. **24**:610, 1915.

2. Rosenow, E. C.: Iritis and Other Ocular Lesions on Intravenous Injection of Streptococci, J. Infect. Dis. **17**:403, 1915.

inflammation caused by the injection of a moderately heavy suspension of bacteria locally may result in panophthalmitis with destruction of the eye. Some of the animals used in the present study acquired septicemia and died during the experimental observations. The bacteria themselves, it was found, are markedly sensitive to oxygen, so that growth during culture occurred only under conditions of reduced oxygen tension. In some instances, aerobic cultivation tends to destroy the characteristics of the organism for elective localization. Then, too, not all dental foci yield micro-organisms which have elective localizing power. Rosenow [3] stated, in this regard, that not every streptococcus has a predilection for the eye. Moreover, he [4] expressed the belief that a prolonged contact of bacteria with leukocytes in the pus and a high oxygen tension in the mucus on the surface of mucous membranes appear to reduce the invasive powers of the bacteria. The length of existence of the bacteria in the host must also be considered. In man it must be assumed that these bacteria were present in the mouth for months and even years, the iris thus being subject to their influence over a long period of stimulation. Finally, it must be remembered that the degree of virulence and the ability to invade tissues will vary under changed conditions of habitat. Other factors of importance that play a role, such as generalized or local lowered resistance of the host, severe or repeated injuries and sensitization of the tissues, are, of course, also to be considered.

Although rabbits are susceptible to the pathogenic action of many bacterial species, one might well argue that positive findings cannot be considered as conclusive evidence of a parallel relation to ophthalmic disease in man. However, Metchnikoff [5] made use of rabbits in his monumental work dealing with phagocytosis, and rabbits are constantly being utilized in laboratories today for both the study and the investigation of various human diseases. Rabbits are susceptible to streptococci and pneumococci and certain of the Spirochaetales in a manner that would suggest a measure of relation between the rabbit and man so far as susceptibility to certain kinds of pathogenic bacteria may be concerned. Furthermore, in those reactions related to a state of hypersensitiveness (e. g., serum sickness) the rabbit displays a capacity for reaction somewhat comparable to that in man.

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3. Rosenow, E. C.: Results of Experimental Studies on Focal Infection and Elective Localization, M. Clin. North America **5**:573, 1921.

4. Rosenow, E. C.: The Pathogenesis of Focal Infection, J. Am. Dent. A. **5**: 113, 1918.

5. Metchnikoff, cited by Garrison, F. H.: History of Medicine, ed. 3, Philadelphia, W. B. Saunders Company, 1924, p. 629.

REVIEW OF THE LITERATURE

Literature Relative to the Clinical Aspects of Iritis and Dental Sepsis.—Among early observers who began to recognize the correlation between iritis and dental infection, Butler,[6] a British ophthalmologist, attached much importance to the part played by infective foci as a cause of iritis. In 1911 this observer stated that iritis is frequently due to toxins absorbed from pus pockets around teeth, in pyorrhea, in sinus infections and from other foci, including those of chronic otorrhea. In his review of 100 cases, he found the iritis in 12 per cent to be due to oral, nasal or other sepsis in and about the mouth. Lang [6] in 1913 found the ocular diseases (not specified as iritis) in 71 of 176 cases to be due to dental infections.

TABLE 1.—*Etiologic Factors in a Study of Two Hundred Cases of Iritis by Irons and Brown (1916 and 1923)*

Infections	Number of Cases of Iritis		Total Number of Cases
	Alone	Associated with Other Infections	
Undetermined	0	7	7
Syphilis	12	26	38
Gonococcus	8	2	10
Tuberculosis	8	0	8
Dental infection	12	15	27
Tonsillar infection	26	27	53
Sinus infection	1	3	4
Genitourinary infection (nonvenereal)	6	0	6
Other infections	3	0	3
No infection	0	0	3
Combined infection	0	41	41
Total number of cases			200

Other pioneers in this field include Irons and Brown,[7] who in 1916 observed a series of 100 cases of iritis in which they considered dental sepsis as a definite factor of importance. In 1923 they [8] observed a second series of 100 cases in which they attached due importance to the role of dental infections. In table 1 are presented the results of their studies with respect to probable etiologic factors, so far as their data permitted.

Fuchs [6] (1924), de Schweinitz [6] (1924), Ball [6] (1927) and Parsons [6] (1929) gave proper importance to dental disease as foci of infections underlying the production of iritis.

Elschnig,[6] in 1925, observing more closely than ever before the possibility of dental sepsis as an etiologic factor, found the iritis in 26

6. Cited by Gifford.[10]

7. Irons, E. E., and Brown, E. V. L.: Etiology of Iritis, J. A. M. A. **66:** 1840 (June 10) 1916.

8. Irons, E. E., and Brown, E. V. L.: Etiology of Iritis, J. A. M. A. **81:** 1770 (Nov. 24) 1923.

per cent of a series of his cases due to this cause. He expressed the belief that a toxemia is produced by the products of disintegrated bacteria and pus present in dental foci.

Among other observers, Bulson [8] (1925) noted that the iritis in 32 per cent of his series of 100 cases was due to infected teeth, whereas Newton [9] (1925), in a series of 75 cases of uveitis, found dental sepsis to be the causative agent in 14.6 per cent. Gifford [10] in 1930 studied the various etiologic factors in a series of 118 cases of iritis; he attributed the infection in 12.7 per cent of these to defective teeth.

It is interesting to note at this point that while Elschnig [6] (1925) believed that a toxemia is caused by the products of disintegrated bacteria and pus present in dental foci, de Schweinitz, in his classic report before the International Medical Congress in 1913, expressed the belief that the production of iritis by bacterial toxins alone had never been proved and that the bacteria themselves are present in the lesions.

That a rather definite correlation exists between iritis and dental sepsis would seem to follow when one considers the curative effects that have ensued after the removal of dental foci. The extraction of the infected tooth or teeth, in some instances with curettage of the alveolar socket for remnants of septic material, resulted in a steady improvement in the eye, with ultimate recovery and no recurrence of the iritis. It seems reasonable to infer that the infective foci were the cause of the inflammation in the eye. The reason why no improvement has seemed to follow the removal of a septic tooth or a number of such teeth in some instances may be that there was incomplete evacuation of all of the diseased tissue. Some observers [11] have called attention to this fact and have reported several cases of iritis in which, though there was no improvement after dental extraction, decided improvement occurred on curettage of the alveolar sockets containing such infective areas.

In some instances the extraction of the infectious foci may, as an immediate result, give rise to acute iritis in an eye that previously had been quiet. In a personal communication Luedde stated (1939) that he had repeatedly noted an apparent focal reaction in ocular tissues when infectious teeth were extracted. In 2 cases the reaction was particularly severe. In 1 of these cases the patient, a man aged 40, had been under treatment elsewhere for recurrent iritis over a period of two years, no

9. Newton, F. H.: Analysis of Series of Cases of Uveitis with Special Reference to Etiology, Texas State J. Med. **21**:315, 1925.

10. Gifford, S. R.: Review of the Literature on the Etiology of Acute Iritis, Am. J. Ophth. **14**:100, 1931.

11. Narreau, O. F.: Relation of Dental Infection to Eye Conditions, Dent. Items Interest **56**:419, 1934. Lowell, W. H.: Relation of Focal Infection to Diseases of the Eye, Dent. Cosmos **76**:350, 1934. de Schweinitz, G. E.: Dental Sepsis in Its Relation to Ocular Disorders, ibid. **62**:565, 1920.

search for foci of infection having been made during this time. Roentgenographic examination revealed the presence of two teeth with considerable peridental infection. Extraction of these was followed by a severe ocular reaction, including diminution of vision, severe pain and clouding of the anterior chamber. After two days the reaction subsided, and the condition cleared up without further recurrence. In the second case, the patient, a woman, first came under observation in 1920, when 40 years of age, for treatment of retinitis pigmentosa. Examination confirmed the previous diagnosis of retinitis pigmentosa and revealed the presence of incipient cataract in both eyes. Thirteen years later, with the subsequent development of the cataractous lenses, iridectomy was carried out on one eye as a preliminary procedure to see how the ocular tissues would react. Mild traumatic iritis followed, but this cleared up spontaneously within a week. Two months later, in preparation for operation for the cataract, a roentgenographic examination of the teeth revealed the presence of peridental infections in eleven. These were extracted at one sitting, immediately after which acute iritis with copious exudation into the anterior chamber occurred (in the eye that was operated on). There were severe pain and elevation of the intraocular tension for several days. This exudate later became organized into a dense grayish mass, filling almost entirely the width and depth of the chamber. Five years later, cataract extraction with removal of the organized exudate from the anterior chamber was attempted. Recovery followed without any such complications as had been precipitated by the multiple extractions several years before.

Literature Relative to Experimental Work Previously Reported.—In 1914 Rosenow [2] pointed out that streptococci from persons with rheumatic arthritis and myositis injected intravenously into animals are prone to lodge in the capillaries of the iris, producing iritis and other ocular lesions. Following this, with a series of animal experiments he was able in 1915 to produce iritis or iridocyclitis in a few instances after the injection of certain laboratory strains of streptococci cultivated from small pus pockets in the tonsils of normal persons.

Irons, Brown and Nadler [12] in 1916 presented a classic work on experimentation with rabbits. Iritis developed in 5 of 8 rabbits into which were injected intravenously suspensions in salt solution (of subcultures on blood agar) of a hemolytic streptococcus isolated from a human tear sac. Cultures of hemolytic streptococci taken from the same tear sac six weeks later failed to produce iritis in a total of 22 rabbits, whether other organisms from a broth culture inoculated directly from

12. Irons, E. E.; Brown, E. V. L., and Nadler, W. H.: The Localization of Streptococci in the Eye: A Study of Experimental Iridocyclitis in the Rabbit, J. Infect. Dis. **18**:315, 1916.

the patient or organisms in pure culture after isolation on blood agar were used for the injections. This loss of virulence seems to indicate that the invasive power of an organism for a special tissue may change within a period of time during residence in the host.

Veach,[13] in 1920, in many series of experiments with rabbits, adopted the procedure of introducing the organisms directly into the anterior chamber. With a fine hypodermic needle, a puncture was made at the corneoscleral margin, the needle going into the base of the iris and as close to its anterior surface as possible, and a saline suspension of the bacteria obtained from patients with septicemia and otitis media and from the pulp of extracted decayed teeth was injected. The organisms used were Staphylococcus aureus, Streptococcus haemolyticus and Streptococcus viridans. In all six series of his report, moderate to severe iritis promptly occurred within twenty-four hours after injection.

Benedict [14] (1920) reported a case in which the patient came under his care because of severe iritis recurring every spring and fall for over a period of six years. These attacks were always preceded by soreness of the right upper bicuspid, which developed about three days before the eye became inflamed. Frequently these attacks were also accompanied by general rheumatic pains, particularly if the patient had been exposed to bad weather. A general physical examination did not reveal any cause for the iritis, except dental infection. The tooth which the patient pointed out as bothersome was extracted, and a culture was made from its pulp. This culture was injected into a rabbit intravenously, after which iritis developed in both eyes within several hours.

Lewis [15] (1923) had a patient with severe iritis who suffered also from an apical abscess; he advised that the offending tooth be removed and cultured in bouillon. The predominating organism found was a "Streptococcus haemorrhagica." He injected massive doses (6 cc.) of this culture intravenously into several white rabbits, and twenty-four hours later he repeated the injections intra-abdominally. He observed a definite iritis (bilateral) within forty-eight hours after the first injection.

Haden [16] (1923) produced iritis and iridocyclitis in rabbits by the intravenous injection of streptococci and staphylococci isolated from chronic dental foci of patients suffering from ocular infections concomitantly and from healthy patients not suffering with concomitant ocular conditions. His observations illustrated, too, that a much higher

13. Veach, O. L.: Experimental Production of Iritis and Its Treatment with Foreign Protein, Am. J. Ophth. **3**:93, 1920.

14. Benedict, W. L.: Value of Dental Examination in the Treatment of Ocular Disorders, Am. J. Ophth. **3**:860, 1920.

15. Lewis, F. P., in discussion on Irons and Brown,[8] p. 1775.

16. Haden, R. L.: Elective Localization in the Eye of Bacteria from Infected Teeth, Arch. Int. Med. **32**:828 (Dec.) 1923.

percentage of ocular lesions occurred in animals inoculated with bacteria which were isolated from those patients suffering from ocular diseases at the time. His case reports showed also that in many instances the iritis and uveitis improved definitely after the removal of the infected teeth.

Brown and Dummer [17] in 1929 worked out a series of experiments in which their technic of administering the organisms showed a distinct line of departure from that of their predecessors. Desiring to establish a more satisfactory method of producing experimental iritis, they discarded the methods used by the aforementioned investigators. They believed that direct injection of the organisms into the eye created too great a source of error to render this method reliable and that the possibilities resulting from trauma and secondary infections were uncontrollable. They thought of intravenous and intraperitoneal injections as too haphazard, believing that secondary foci might be initiated which would change the characteristics of the organism or cause a generalized infection that would kill the animal before the desired localization took effect. They adopted the direct arterial route, dissecting the neck of the animal to free the carotid artery from its adnexae and injecting about 1 cc. of a heavy suspension of organisms directly into this vessel. Iritis was produced in twenty-four hours in 2 of 3 rabbits into which a strain of hemolytic streptococcus from the nasal secretions of a patient suffering from acute iritis was injected.

Brown [18] (1932) claimed to have produced an acute inflammation of the uveal tract by the intraocular injection of a streptococcus toxin associated with scarlet fever. He did not, however, experiment with any toxins obtained from bacteria associated with dental infections.

Berens, Nilson and Chapman [19] in 1936 produced iritis in rabbits by the intravenous injection of either primary or purified cultures obtained from various foci, such as the nose and throat, teeth and tonsils of patients with acute or chronic ocular inflammations, arthritis and thyrotoxicosis and, in some instances, of healthy subjects without demonstrable lesions. The organisms identified in the pure cultures consisted of staphylococci (Staph. albus and aureus), streptococci (alpha, beta and gamma types), enterococci, colon bacilli, nonlactose fermenters and Friedländer bacilli.

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17. Brown, A. L., and Dummer, C.: The Experimental Production of Iritis, Arch. Ophth. **2**:573 (Nov.) 1929.

18. Brown, A. L.: Considerations Underlying the Experimental Production of Iritis, Am. J. Ophth. **15**:19, 1932.

19. Berens, C.; Nilson, E. L., and Chapman, G. H.: Iritis Produced in Rabbits' Eyes by Intravenous Injection of Bacteria Isolated from Patients with Certain Inflammatory Eye Diseases, Am. J. Ophth. **19**:1060, 1936.

One must not lose sight of the fact that while some research has been done on the question of dental foci and iritis, most investigators have concerned themselves only with the micro-organisms present in the dental lesions and few have considered the investigation of the effects of bacterial toxins produced in and about such dental foci.

PROCEDURE OF EXPERIMENTS

In order to ascertain the effects of bacteria and the bacterial toxins which are associated with dental infections on the iris of laboratory animals, the following experiments were performed. They were divided into five series, three concerned with the effects of toxins alone and the others with the organisms themselves. A general scheme of the entire experimental work is presented in table 2, which, it is hoped, will serve as a guide from time to time throughout the work.

TABLE 2.—*General Scheme of Experiments*

Series of Experiment	Material Used in Administration	Presence or Absence of Concomitant Iritis in Patients from Whom Teeth Were Obtained
1	Bacterial toxin A	Without iritis
2	Bacterial toxin B	Without iritis
3	Bacterial toxin C	With iritis
4	Bacterial organisms (suspension A)	Without iritis
5	Bacterial organisms (suspension B)	With iritis

The chief interest has centered, however, on whether or not the toxins alone were responsible for the ocular manifestations rather than the micro-organisms proper. Many previous investigators who have produced iritis in laboratory animals made use of virulent organisms obtained from various body foci. I wished to see, aside from this, what effect particularly the bacterial toxins from dental foci alone would have on the eye.

SERIES 1.—*Injections with Bacterial Toxin A.*—Twenty-four teeth were obtained in the dental clinic under aseptic precautions immediately after their extraction from patients who had no demonstrable ocular lesions at the time. The condition of the teeth obtained throughout these experiments (both from clinical and from roentgenographic evidence) was as follows: Several had rarefied areas around their apexes: several had been loose in their sockets and contained suppurative processes at the gum margins; several contained loose bulbous granulomas around their apexes; some were abscessed, and a few had infected root canals; in a few instances retained roots which had been left in the lower cuspid and bicuspid regions were obtained.

With a sterile rongeur forceps, the tips of the apexes of these teeth were cut from the main root stem (including the root canals however) and dropped into a small Erlenmeyer flask containing 25 cc. of sterile beef infusion broth. Beef broth was used in the beginning because the organisms present did not seem to

require especially nutritive mediums. After its contents were shaken vigorously for several minutes, the flask was placed in the incubator for three to four days to allow for bacterial growth and activity and for the production of exotoxins. Meanwhile, cultures of this suspension on blood agar plates revealed the following organisms to be present: nonhemolytic streptococci; nonhemolytic staphylococci; nonhemolytic hemophili; hemolytic hemophili, and Str. viridans.

At the end of the period of incubation, the entire suspension, containing apexes, granulomatous material, spicules and material curetted from the root surfaces, was filtered clear and the filtrate placed over a water bath at 60 C. for one hour in order to kill the organisms present. Subsequent subcultures from this proved that no live organisms were present.

TABLE 3.—*Results Obtained with Toxin A*

Method of Administration	Ocular Involvement	Other Forms of Involvement
Subconjunctival injections in rabbits 1, 2, 3 and 4 with increasing doses of 2 to 8 minims, respectively	No signs of iritis; suppurative conjunctivitis in rabbits 3 and 4	None
Subconjunctival injections in rabbits 1, 2, 3 and 4 with uniform doses of 1 cc. every 48 hours	No signs of iritis; suppurative conjunctivitis in rabbits 1 and 2	None
Subcutaneous injections in rabbits 2 and 4 of 2 cc. every 48 hours	None	None
Intradermal injections in rabbits 1, 3, 5 and 6 of 0.5 cc. into the skin over the neck	None	Mild local erythema of the skin persisting 18 to 36 hours
Intravenous injections in rabbits 1, 3, 5 and 6 of doses of 1.5 cc.; injections repeated	None	Rabbit 5 became quite ill for 3 to 4 days
Instillations into the conjunctival sac alone in rabbits 1, 3 and 5	None	None
Instillations into the conjunctival sac combined with physostigmine salicylate in rabbits 2, 4 and 6	None (marked pupillary contraction)	Systemic reactions of marked tremors of the body and leg, due to poisoning from physostigmine salicylate
Instillations into the conjunctival sac with injury to the iris in rabbits 1, 3 and 5	No signs of iritis; slight ciliary redness over the site of the needle puncture	None

The resultant suspension was designated as toxin A for purposes of identification and investigated for its experimental effects.

Four healthy albino rabbits, weighing approximately 2,000 Gm. and from stock previously unaffected by immunization or sensitization experiments, were given a subconjunctival injection of toxin A in the right eye, the dosage varying from 2 minims (0.12 cc.) for the first rabbit to 8 minims (0.49 cc.) for the fourth, with increases of 2 minims for each succeeding animal. Before each injection, the conjunctival sacs were instilled several times with a 1 per cent solution of pontocaine hydrochloride and the sac flushed out with saline solution. The left eye of each rabbit was used as a control.

Observations were made in four, eight, twelve, twenty-four and forty-eight hour periods in each case. At the end of the twenty-four hour period, a mild to moderately severe suppurative conjunctivitis developed in rabbits 3 and 4, which cleared up spontaneously in two or three days. No signs of iritis appeared at any time throughout these periods (table 3).

The foregoing procedure was repeated for the same 4 rabbits after one week's rest, an increased amount (1 cc.) being used for the injections, which were repeated every forty-eight hours for three administrations. As in the previous experiment, no signs of iritis developed at any time, although a mild conjunctivitis developed in rabbits 1 and 2, which spontaneously cleared up within a few days. At no time were any of the animals observed to be ill.

To test the potency of the toxin suspension, rabbits 1 and 3 of this series and 2 others from a fresh stock were given intradermal injections of 0.5 cc. of the toxin into a shaved area on the back of the neck. A mild local cutaneous reaction, consisting of a moderately large circular erythematous area (about the size of a 5 cent piece), developed in all 4 rabbits; it resolved within two days. Similar injections made with sterile beef broth infusion in the same amounts failed to elicit a similar cutaneous reaction.

To ascertain whether or not the subcutaneous route of administration could be effective, rabbits 2 and 4 were given subcutaneous injections of 2 cc. of the toxin every two days for several administrations. No signs of iritis appeared (table 3).

It was then decided to administer the toxin suspension intravenously, using 2 of the original rabbits (nos. 1 and 3) and 2 from a fresh stock (nos. 5 and 6). Animals 1 and 5 each received 1 cc. intravenously in the vein of the right ear, and animals 3 and 6 each received 1.5 cc. in the vein of the right ear. At no time did any signs of iritis develop, though rabbit 5 became ill at the end of twenty-four hours, but recovered. Repetition of the injections in the same amounts after one week's rest did not produce any positive results.

It was next decided to try the effects of the toxin A on the iris by direct instillation into the conjunctival sac: first, alone; secondly, in conjunction with the instillation of physostigmine salicylate, and thirdly, in conjunction with direct irritation (trauma) to the iris by means of a sterile needle. The reason for using the physostigmine salicylate with the toxin was to observe if the combined effects of the two would more readily produce iritis. The strong contraction of the pupil, it was thought, during the presence of the toxin might well serve to initiate the inflammatory activity of the iris.

All 6 rabbits in this group were used throughout these procedures. The right eyes were used for the administration of the toxin and physostigmine salicylate, the left eyes being left as controls. The toxin was instilled every day for a ten day period in rabbits 1, 3 and 5, while rabbits 2, 4 and 6 received both instillations of toxin and drops of 1 per cent aqueous solution of physostigmine salicylate. About 3 to 5 drops of toxin and 1 to 2 drops of physostigmine salicylate from the end of a fine dropper were used. Observations were made two or three times each day during the course of this experiment, and at no time did any signs of iritis appear in any of the 6 animals. On the first day rabbits 2, 4 and 6 suffered from the effects of poisoning with the physostigmine salicylate, due obviously to an overdose. The original dose (3 to 5 drops) was reduced thereafter, and no further disturbing effects from this drug were noted (table 3).

After studying the combined effects of toxin and physostigmine salicylate, it was decided to investigate the combined effects of toxin and direct irritation of the iris. After a week's rest, the same 6 animals were used, as follows: Rabbits 2, 4 and 6 received daily instillations in the right eyes of 2 to 5 drops of toxin A suspension, while rabbits 1, 3 and 5 likewise received daily instillations of toxin in the right eyes plus direct irritation of the iris of the same eyes every other day. The latter procedure was accomplished as follows: Four to 6 drops of a 1 per cent solution of pontocaine hydrochloride was dropped over the cornea into the sac, followed a few minutes later with a copious flush with saline solution through the entire sac. The tip of a small sterile needle, fixed into a wooden handle, was

admitted through the upper and outer limbus directly into the anterior chamber and in front of the plane of the iris; its point was then drawn over the base of the iris to and fro for a few strokes and quickly withdrawn. A small spot of ciliary redness appeared at the site of entry of the needle shortly after and remained for several hours, but later disappeared. The trauma to the iris was repeated in the 3 animals mentioned every other day for four times, but except for the small amount of ciliary redness appearing only at the site of puncture, which was considered merely the immediate result of the needle passing through tissue, no definite signs of iritis appeared at any time throughout this series. The pupil remained always well reactive, equal in size to its fellow and regular in shape. The iris itself appeared normal when compared with its fellow. At no time did the faint redness appearing in scattered areas of the surrounding conjunctiva assume the dignity of a true circumcorneal injection (table 3).

TABLE 4.—*Results Obtained with Toxin B*

Method of Administration	Ocular Involvement	Other Forms of Involvement
Subconjunctival injections in rabbits 1 and 2 of 1 cc. of toxin	No signs of iritis; suppurative conjunctivitis in rabbits 1 and 2	None
Subconjunctival injections in rabbits 1 and 2, after 1 week rest, of 1 cc. of toxin every 48 hours	None	None
Intradermal injections of 0.5 cc. in rabbits 1 and 3	None	Local erythema of the skin 28 to 48 hours
Subcutaneous injections in rabbits 1, 2 and 3 of 2 cc. every 48 hours	None	None
Intravenous injections in rabbits 1, 2 and 4 of 1 cc. of toxin; repeated after 48 hours in the same animals with 2 cc.	None	Rabbit 4 became severely ill after 2d dose and died 5 days later
Instillations into the conjunctival sac alone in rabbits 1, 2, 3 and 4	None	None
Instillations into the conjunctival sac in combination with physostigmine salicylate in rabbits 2 and 4	None (marked pupillary contraction)	None
Instillations into the conjunctival sac with injury to the iris in rabbits 2 and 4	No signs of iritis; slight ciliary redness over the site of the needle puncture	None

SERIES 2.—*Injections with Bacterial Toxin B.*—Since all negative results were obtained with the toxin made for the first series of experiments, it was decided to prepare a new supply from other dental material, using a different culture medium and method of extracting the toxin, which was designated as toxin B for identification.

Twenty teeth were again obtained in the dental clinics from patients who at the time manifested no ocular inflammation. Under aseptic precautions, these were prepared in a similar manner as before, except that 40 cc. of brain-heart infusion broth containing 0.1 per cent agar was used for the medium. This was considered more suitable as a medium for organisms that might not only require especially nutritive material for growth and activity but also be micro-aerophilic in their oxygen requirements.

Into each of two sterile test tubes, approximately 20 cc. (in order to give depth to the culture bed) of the freshly made suspension was poured and incubated for three to four days. Cultures made during this time showed the presence of the following organisms: hemolytic streptococci; Str. viridans; non-

hemolytic streptococci; hemolytic hemophili (pleomorphic gram-negative rods) and nonhemolytic hemophili; nonhemolytic staphylococci, and gram-positive spore bearers (aerobic).

The bacteria in one of these test tubes was then subjected to the water bath at 60 C. for one hour. Cultures of this subsequently proved sterile. The contents of the second test tube were passed through a Berkefeld filter, and cultures of the filtrate later proved also to be sterile. The resultant suspension and filtrate were then added to each other, mixed and labeled toxin B for further identification.

Four healthy albino rabbits selected from a stock previously unaffected by immunization experiments were used in this series. The results obtained are tabulated for clarity and convenience in table 4.

In order to avoid the repetitious use of terms and the voluminous details of procedure in the administration of the toxins and suspensions of bacteria and to present the experimental data in as clear and understandable a manner as possible, it was deemed advisable to make tabulations of all results obtained at the end of each new experimental series (similar to the manner shown in table 3). The amounts used in the injections were practically identical with those used previously. All details and steps in administration were the same. Right eyes were always used for the local injections and the left eyes for controls.

SERIES 3.—*Injections with Bacterial Toxin C.*—Having obtained negative results thus far with bacterial toxins associated with septic dental processes from patients unaffected at the time with ocular inflammation, I then proceeded to investigate the effects of toxin which was obtained from dental foci in patients who did manifest uveal inflammation at the same time.

The first patient, a woman aged 48, came to the clinic with a markedly acute iritis of the left eye and a large corneal ulcer; the onset occurred without an apparent external cause and was followed one week later by involvement of the other eye. General work-up in the various departmental clinics and laboratory tests gave essentially negative results, except for four upper incisors which were extremely loose in their sockets and showed greenish suppurative processes around the gum margins. Roentgenograms showed the presence of rarefied areas in the region of two apexes. Extraction of all four offending teeth was followed in one week by marked improvement in both eyes, with total disappearance of symptoms in the original eye.

The second patient, a man aged 36, previously in excellent health, had acute iritis in the right eye which had developed without apparent cause. Clinical and laboratory examinations gave essentially negative results. External examination of his teeth showed the presence of one upper cuspid to be extensively involved with ulceration. A roentgenogram indicated one small area of bone absorption near the apex. Removal of this tooth after one week's unsuccessful treatment with the usual methods resulted in prompt recovery.

The third patient, a man of about 69, came to the ophthalmic clinic with acute iridocyclitis of the right eye, with pus in the anterior chamber and ulceration of the cornea. Rigid treatment included, among other measures, the removal of several teeth, various states of caries, abscesses, retained roots and suppurative processes at the gum margins being present. Examination revealed the presence of an infection of an antrum, chronic prostatitis and hypertension. Improvement followed dental treatment, and the clearing up of other foci was rather protracted. Eventually, after several months of rigid care, the corneal ulcer healed and the ocular inflammation subsided.

From the teeth extracted from these three persons a toxin (C) was prepared in the manner similar to that worked out in the second series, viz., by using brain-

heart infusion broth with 0.1 per cent agar and extracting the toxin by passing the three to four day old bacterial suspension through a Berkefeld filter. Individual preparations of toxin were made, of course, in each instance as the patient came to the clinic for treatment; but since all methods of preparation and subsequent administration of the toxins were repeated in identical fashion, I have, for purposes of brevity and clarity, combined the data into one composite group (table 5).

Bacterial cultures made at the time of this group showed the following organisms predominating: gram-positive spore bearers (aerobic); nonhemolytic staphylococci; nonhemolytic streptococci; pleomorphic gram-negative rods (hemolytic hemophili); hemolytic streptococci and alpha hemolytic streptococci (Str. viridans).

TABLE 5.—*Results Obtained with Toxin C*

Method of Administration	Ocular Involvement	Other Forms of Involvement
Subconjunctival injections in rabbits 1 and 2 of 1 cc. of toxin	No signs of iritis; mild suppurative conjunctivitis in rabbits 1 and 2	None
Subconjunctival injections in rabbits 1 and 2, after 1 week's rest of 1 cc. of toxin every 48 hours	None	None
Intradermal injections of 0.5 cc. in rabbits 1 and 3	None	Local erythema of the skin persisting 2 days
Subcutaneous injections in rabbits 1, 2 and 3 of 2 cc. every 48 hours	None	None
Intravenous injections in rabbits 1, 2 and 4 of 1 cc. of toxin; repeated after 48 hours in the same animals with 2 cc.	None	Rabbit 4 became somewhat ill but recovered
Instillations into the conjunctival sac alone in rabbits 1, 2, 3 and 4	None	None
Instillations into the conjunctival sac in conjunction with physostigmine salicylate in rabbits 2 and 4	None (marked pupillary contraction)	None
Instillations into the conjunctival sac with injury to the iris in rabbits 2 and 4	No signs of iritis; slight ciliary redness over the site of the needle puncture	None

Four healthy albino rabbits selected from a stock previously unaffected by immunization experiments were used in this series of experiments with toxin C. Amounts and methods of administration were the same as in series 2, the right eyes being used for instillations and injections and the left eyes for controls. The results are tabulated in table 5.

SERIES 4 AND 5.—*Injections with Bacterial Suspensions A and B.*—I wish next to confirm some of the positive results obtained by previous investigators in the production of experimental iritis in animals with bacterial organisms. Of the various routes of administration that presented themselves for consideration, I decided on two as the most desirable, viz: (1) direct intraocular implantation and (2) intravenous. For the intraocular technic, I followed the method of Veach,[13] who made injections into the limbus with a fine hypodermic needle, going into the base of the iris and as close to its anterior surface as possible. This procedure was preceded with local anesthesia followed with a copious lavage of the conjunctival sac with saline solution, the latter being repeated after the injection was completed. For the intravenous injections, moderate (1.5 cc.) to heavy (3 cc.) doses of the bacterial suspensions were used.

The organisms used were obtained from twenty-four hour subcultures of the primary growth made during the second and third series of experiments. These consisted of two main groups: those obtained from dental foci in patients not

TABLE 6.—*Results with Injections of Bacterial Suspension A (From Foci of Patients Without Concomitant Iritis)*

Method of Administration	Ocular Involvement	Other Forms of Involvement
Intraocular injections of 0.2 cc. of suspension of organisms at the base of the iris in rabbits 1 and 1x*	Marked iritis appearing within 8 hours and persisting for several days; resolution on the fifth day	None
Intravenous injections in rabbits 2 and 2x of 1.5 cc. of suspension of organisms A	None	None
Intravenous injections in rabbits 1 and 2 of 3 cc. dosage (increased)	Moderate iritis appearing within 12 hours in both rabbits and disappearing on the second day	None
Intravenous injections in rabbits 1x and 2x of 3 cc. dosage (increased)	Moderately severe iritis appearing within 8 hours in both animals, in 2x greater than in 1x; resolution within 2 days	None

* Numerals without x signify freshly selected animals not previously given injections of proteins in these experiments. Numerals with x affixed thereto signify animals previously given injections of proteins in these experiments.

TABLE 7.—*Results with Injections of Bacterial Suspension B (From Foci of Patients with Concomitant Iritis)*

Method of Administration	Ocular Involvement	Other Forms of Involvement
Intraocular injections of 0.2 cc. of suspension of organisms at the base of the iris in rabbits 3 and 3x	Marked iritis in both rabbits within 6 hours, persisting for several days and resulting in panophthalmitis	None
Intravenous injections in rabbits 4 and 4x of 1.5 cc. of suspension of organism B	Ciliary redness in both rabbits in 8 to 12 hours with resolution at the end of 24 hours	None
Intravenous injections in rabbits 3 and 4 of 3 cc. dosage (increased)	Mild to moderately severe iritis in both rabbits after 8 hours with resolution in rabbit 3 after the second day; infection persisted in rabbit 4 until the third day	Both rabbits became slightly ill within 12 hours; but recovered
Intravenous injections in rabbits 3x and 4x of 3 cc. dosage (increased)	Mild iritis in rabbit 4x after 12 hours; disappeared in 2 days; marked iritis in rabbit 3x within 12 hours, persisting for 2 to 3 days	Rabbit 3x became ill after first day; grew worse and died on sixth day

suffering from demonstrable uveal inflammations at the time and those obtained from dental foci in patients with concomitant iritis. For purposes of identification, the former was called bacterial suspension A and the latter bacterial suspension B. The bacterial contents of group A corresponded in identity to those used in the second series of toxin B experiments, while the bacterial contents of group B corresponded in identity to those used in the third series of experiments with

toxin C. A review of the general scheme of experiments (table 2) at this juncture will illustrate this.

For these last two series, a total of 8 animals was used: 4 healthy albino rabbits (nos. 1, 2, 3 and 4) selected from a stock previously unaffected by immunization or sensitization experiments and 4 healthy rabbits (nos. 1x, 2x, 3x and 4x) selected from those used in the earlier experiments and subjected to injections of toxin intravenously. The reason for using the latter was to see what effect, if any, the injection of organisms would produce in animals previously subjected to injections of protein.

The results in both these final series of experiments are tabulated in tables 6 and 7, respectively. All positive results were checked by repeating the procedures involved with sterile brain-heart infusion broth (without organisms or toxin) and obtaining negative results therefrom.

SUMMARY AND CONCLUSIONS

Iritis failed to develop in albino rabbits subjected by various routes of administration to the effects of bacterial toxins associated with septic dental foci in man.

Bacterial toxins obtained from septic dental foci of patients either with or without concomitant iritis did not cause iritis experimentally in the rabbit.

The route of administration of the bacterial toxins did not alter their effects, except to produce general illness and death in a few rabbits when given in large doses by the intravenous method.

On the other hand, the administration of bacterial organisms associated with septic dental foci in man produced iritis in albino rabbits.

It seems possible that the bacterial strains obtained from patients who had concomitant iritis possess greater virulence than those obtained from patients without concomitant inflammation of the iris.

In rabbits previously given injections of bacterial toxin iritis subsequently developed when bacteria was injected.

It is evident that the cause of the inflammation of the iris in these animals is directly due to a bacterial attack on the tissue. The inflammation could not be reproduced by administration of bacterial products such as the toxins made in this experiment.

These experiments do not refute the concept that in man the production of iritis may be brought about as follows: Toxins diffusing into the blood stream from an active septic focus or foci in the body might sensitize the iris tissue during a period of months or years, so that subsequently when bacterial emboli, discharged into the blood stream from this same (primary) focus, chance to lodge in the capillaries of the iris they (emboli) find a conditioned field, enabling them to manifest their pathogenic potentialities.

Miss Helen K. Moran, of the department of bacteriology of the Firmin Desloge Hospital, assisted in the preparation of the bacteriologic material for these experiments.

ACCEPTANCE OF WEAK CYLINDERS AT PARADOXIC AXES

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I have often noted, and no doubt a similar observation lies within the experience of every oculist, that after determining at retinoscopic examination that the patient needs a weak cylinder with its axis horizontal, the patient decidedly prefers the cylinder at an angle exactly opposite; however, with the addition of more spherical correction, he promptly reverses his choice to the correct meridian. This reversal phenomenon does not occur when the true axis is in the vertical or oblique meridians.

I do not refer to cases of astigmatism in which a weak plus cylinder becomes converted into an equivalent minus cylinder at the opposite axis as the result of an accommodative effort on the part of the ciliary muscle. I refer to instances in which cyclopegia is well effected by homatropine or atropine and in which the question of accommodation does not enter and the sign of the cylinder remains unchanged.

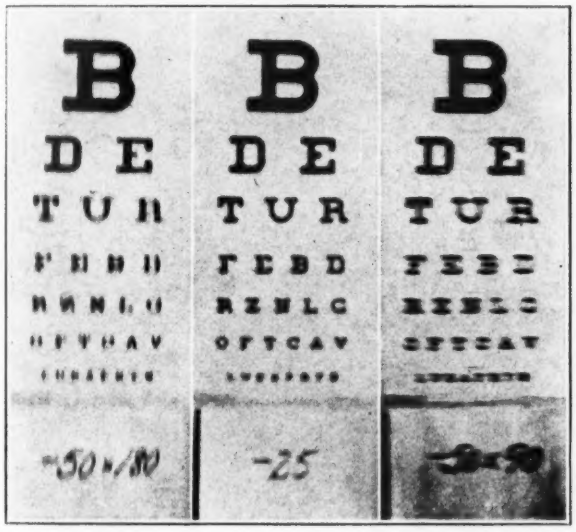
The explanation of this phenomenon lies in the following partially known facts: The average test letter is more readily recognizable when the vertical components are clear and the horizontal components blurred than when there is a lesser but uniform blur of all the elements. The letter is least recognizable when the horizontal components are clear and the vertical components blurred.

It must be remembered that in the eye the vertical curvature of the cornea-lens system is responsible for the clarity of the horizontal elements of the test letters, while the horizontal curvature influences the proper focusing of the vertical components of the letters. Blurring of these components as they appear to the eye may be simulated by camera studies. The distortion produced by lenses before the focused camera is not exactly equal to the distortion of the retinal image that these same lenses would produce if placed before an atropinized emmetropic eye, but the differences are sufficiently small to permit the analogy. Placing a cylinder at axis 90 degrees before the eye changes the effective horizontal curvature.

From the Knapp Memorial Eye Hospital.

Figure 1 *A* shows the effect obtained with an otherwise perfectly focused camera by placing in front of it a —0.50 D. cylinder, axis 180 degrees. This distorts the horizontal components of the letters because it decreases the vertical curvature of the lens system. The horizontal curvature remains in focus, giving clarity to the vertical components of the letters. This effect is comparable to that produced by a simple hyperopic astigmatism of + 0.50 D., axis 180 degrees.

Figure 1 *B* shows a setup with a — 0.25 D. sphere in front of the camera. It will be noted that the 20/20 line is slightly less legible than in figure 1 *A*, notably the letters A, R, and N. Holding the photograph at arm's length makes this more evident. This effect is comparable to that produced by a hyperopia of + 0.25 D.



A B C

Fig. 1.—*A*, horizontal elements blurred 0.50 D.; vertical elements in focus. This effect is comparable to that produced by a refractive error of + 0.50 D., axis 180 degrees. *B*, horizontal and vertical elements both blurred 0.25 D. This effect is comparable to that produced by a refractive error of + 0.25 D. *C*, vertical elements blurred 0.50 D.; horizontal elements in focus. This effect is comparable to that produced by a refractive error of + 0.50 D., axis 90 degrees.

Figure 1 *C* shows the effect of a —0.50 D. cylinder held at 90 degrees in front of the focused camera. The legibility is much less than in figure 1 *A* and *B*, because the vertical components are blurred. This effect is comparable to that produced by a simple hyperopic astigmatism of + 0.50 D., axis 90 degrees.

Figure 2 shows diagrammatically the focal planes of the vertical and horizontal corneal curvatures in their relation to the retina, *R*, in a

case of hyperopic astigmatism (+ 1 D. sphere ⊃ + 0.25 D. cylinder, axis 180 degrees) when there is no lens in front of the eye (fig. 2 *A*); when the spherical correction is deficient by 0.25 D. and there is no cylindric correction (fig. 2 *B*); when the spherical correction is deficient by 0.25 D. and the cylinder is at the proper axis, 180 degrees (fig. 2 *C*), and when the spherical correction is deficient by 0.25 D. and the cylinder is at the improper axis, 90 degrees (fig. 2 *D*). Each space between the dots represents 0.25 D.

The effect of the correction in figure 2 *C* may be reproduced on the focused camera by a —0.25 D. sphere superimposed (fig. 1 *B*).

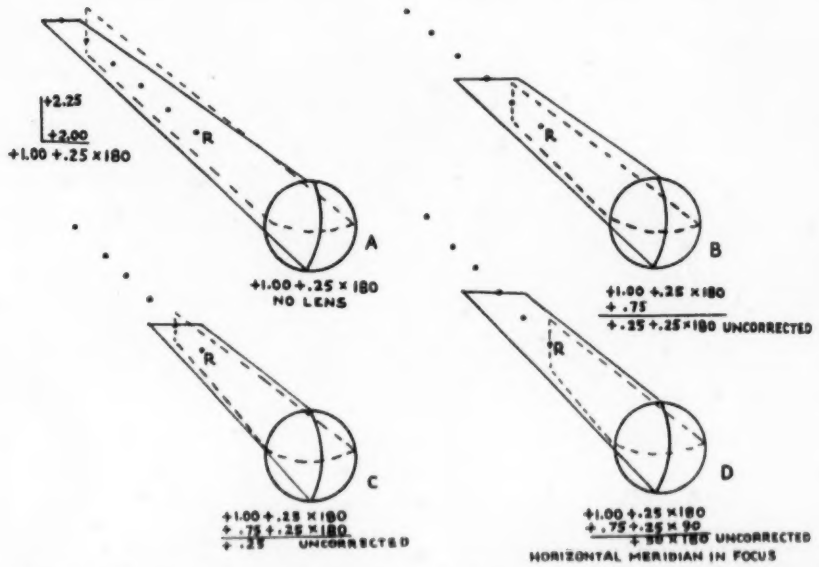


Fig. 2.—Diagrams representing the focal planes of the vertical and horizontal corneal curvature in their relation to the retina in a case of hyperopic astigmatism (+ 1 D. sphere ⊃ + 0.25 D. cylinder, axis 180 degrees) in various stages of correction. The partial correction in figure 2 *C* produces an effect comparable to that in figure 1 *B*. The partial correction in figure 2 *D* produces an effect comparable to that in figure 1 *A*. Given the choice between the correction in figure 2 *C* and that in figure 2 *D*, a patient may choose that in figure 2 *D*, wrong axis.

The effect of the correction in figure 2 *D* may be reproduced on the focused camera by a —0.50 D. cylinder, axis 180 degrees (fig. 1 *A*).

The patient in this particular case, having an undercorrected spherical error, may, when confronted with a choice of cylinder at the right axis (180 degrees, as in figure 2 *C*) and the wrong axis (90 degrees, as in figure 2 *D*), at times choose the wrong axis, because the vertical components of the letters are then in focus. With the addition of 0.25 D. more spherical correction, he will reverse his choice to 180 degrees.

Figure 3 shows diagrammatically the focal planes of the vertical and horizontal corneal curvatures in relation to the retina, *R*, in a case of hyperopic astigmatism (+ 1 D. sphere ⊃ + 0.25 D. cylinder, axis 90 degrees) when there is no lens in front of the eye (fig. 3 *A*); when the spherical correction is deficient by 0.25 D. and there is no cylindric correction (fig. 3 *B*); when the spherical correction is deficient by 0.25 D. and the cylinder is at the proper axis, 90 degrees (fig. 3 *C*), and when the spherical correction is deficient by 0.25 D. and the cylinder is placed at the improper axis, 180 degrees (fig. 3 D).

The effect of the correction in figure 3 *C* may be represented by figure 1 *B*, and that in figure 3 *D*, by figure 1 *C*. The patient in this case,

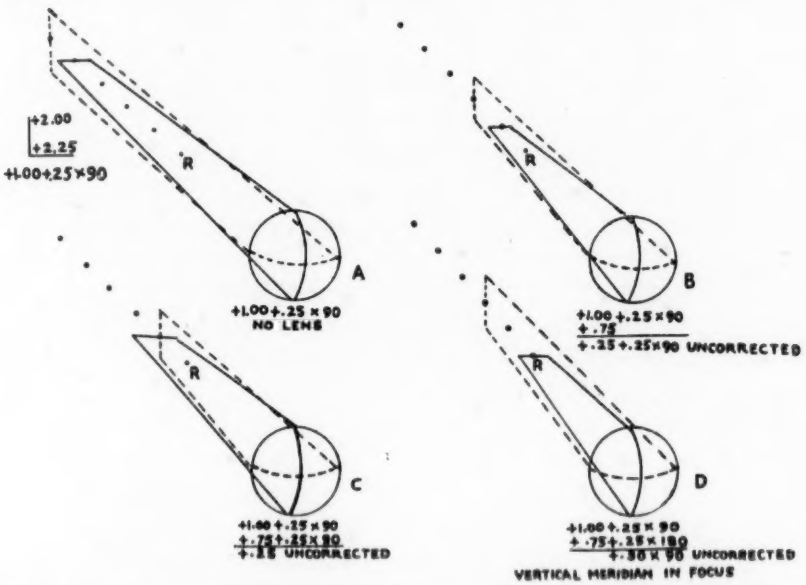


Fig. 3.—Diagrams representing the focal planes of the vertical and horizontal corneal curvatures in their relation to the retina in a case of hyperopic astigmatism (+ 1 D. sphere ⊃ + 0.25 D. cylinder, axis 90 degrees) in various stages of correction. The partial correction in figure 3 *C* produces an effect comparable to that in figure 1 *B*. The partial correction in figure 3 *D* produces an effect comparable to that in figure 1 *C*. Given the choice between the correction in figure 3 *C* and that in figure 3 *D*, a patient will choose that in figure 3 *C*, right axis.

although having an undercorrected spherical error, will choose the proper axis (90 degrees), as in figure 3 *C*, and will reject the improper one (180 degrees), as in figure 3 *D*, because the vertical components of the letters are then out of focus. The addition of more spherical correction to make up for the deficiency will improve his visual acuity and will confirm the choice of axis 90 degrees.

A similar set of diagrams may be constructed for a myope with a weak cylinder at 180 degrees and at 90 degrees, except that the focal planes of the corneal curvatures will lie in front of the retina.

Suppose at refraction a myope requires a cylinder of —0.25 D., axis 180 degrees, and the spherical error is undercorrected by —0.25 D. If the cylinder is placed in the proper axis, the patient sees just as a person with uncorrected myopia of —0.25 D. sees. If the cylinder is turned to the improper axis of 90 degrees, the vertical corneal curvature is undercorrected by 0.50 D., but the horizontal curvature is made emmetropic, causing the upright components of the letters to stand out clearly. This is frequently more acceptable to the patient than the uniform blur present with myopia of —0.25 D., and he will demand the wrong axis. The addition of a —0.25 D. sphere will cause the patient to reverse his choice of cylinder to one at the proper axis of 180 degrees.

Suppose a myope requires a cylinder of —0.25 D. at axis 90 degrees. With the spherical error undercorrected by 0.25 D., placing the cylinder at the correct axis of 90 degrees will leave a spherical myopia of —0.25 D. Rotating the cylinder to 180 degrees will undercorrect the horizontal corneal curvature by 0.50 D. but will fully correct the vertical corneal curvature. The horizontal components of the letters will stand out clearly, while the upright parts will remain blurred. This is by no means as acceptable to the patient as the uniform blur of the myopia of —0.25 D. when the cylinder is placed at axis 90 degrees, and he will not demand the wrong axis. Adding the —0.25 D. sphere confirms the choice of axis at 90 degrees.

Both hyperopes and myopes, then, who on retinoscopic examination are shown to require a 0.25 D. cylinder, axis 180 degrees, may, and frequently do, choose the cylinder at axis 90 degrees if their spherical error is undercorrected by 0.25 D. If the deficiency in the spherical correction is added, the cylinder is promptly accepted at 180 degrees. In order for the cylinder when placed in the wrong axis to cause full correction of the horizontal corneal curvature, the sphere must be deficient by an amount equal to the strength of the cylinder.

If a hyperope or a myope requires a 0.25 D. cylinder, axis 90 degrees, as shown by retinoscopic examination, he is not likely to accept the cylinder at the wrong axis (180 degrees) even though the spherical error is undercorrected by 0.25 D.

This reversal phenomenon of the cylinder is met most frequently in myopes with an astigmatic error of 0.25 D. or 0.50 D. in the horizontal axis. It is apparent that in such cases the spherical error has to be fully corrected before reliance can be placed on the choice of axis.

A cylinder of 0.75 D. or more at axis 18 degrees is not likely to be accepted at a contradictory axis for two reasons. First, the refractionist

is not likely to undercorrect the spherical error by 0.75 D. or more; as I have noted previously, one of the conditions of the phenomenon calls for a deficiency in the amount of the sphere equal to the strength of the cylinder. If the sphere is deficient by an amount less than the strength of the cylinder, neither meridian will be in focus and the patient will not definitely accept either axis. Second, if the corrective cylinders were offered the patient while the spherical correction was deficient by 0.75 D. or more, the images would be so blurred for both the proper and the improper axes that he would accept neither axis very decisively.

When the cylinder lies at 45 or 135 degrees and the patient's spherical error is undercorrected, he will always accept the proper axis, because a 0.25 D. spherical deficiency will be preferred to the distortion produced by a 0.50 D. cylinder at 135 and 45 degrees. The closer the cylinder lies to 180 degrees the more likely is the occurrence of the reversal phenomenon.

One does not often encounter this phenomenon in hyperopes because one always starts refraction with a high plus sphere and works downward; by so doing one is not likely to undercorrect the spherical error. If undercorrection does occur, the phenomenon will be noted, unless, of course, the patient accommodates to make up for the lack of plus sphere, in which event he will, for the time being, have full spherical correction. Often some accommodative ability persists to mask the reversal phenomenon. It will, however, be noted with adequate cycloplegia.

For myopes, one proceeds from low to higher spheres and thus starts with an undercorrection. This, of course, tends to bring out the reversal phenomenon.

The myope who is wearing a slight spherical undercorrection will utilize the principles of letter recognition mentioned by looking at distant type through the sides of his lenses. He produces thereby a vertical astigmatic effect in the spheres and renders the horizontal corneal curvature more nearly emmetropic. This causes the legibility to be improved, because it clarifies the vertical moieties of the letters. With lenses of -2.00 to -4.00 D. of the old uncompensated type, this peripheral astigmatism may amount to 0.50 or 0.75 D. The subject will not peer through the upper or the lower edges of the lenses, as this will cause the induced cylinders to lie in axis 180 degrees, emphasizing the less desirable horizontal components.

COMMENT

Astigmats with a cylinder of 0.25 or 0.50 D. in the horizontal axis and a sphere which is deficient, respectively, by 0.25 or 0.50 D. will often accept the cylinder at the opposite axis (90 degrees). When

restitution of the deficiency in the spherical correction is made, the patient will demand the proper axis.

When the true axis lies at 90 degrees, this reversal phenomenon does not occur.

I occasionally utilize the reversal phenomenon to check for overcorrection of sphere in myopic astigmatism, axis 180 degrees, when the cylinder is a weak one. If on reversing the sphere proportionately the cylinder is not accepted at the improper axis of 90 degrees, it is an indication that the spherical correction was too high originally.

The optical basis of this reversal phenomenon has been illustrated. It involves the comparative ease of recognition of test letters when the vertical or horizontal components are blurred as compared with a lesser but uniform blur of all the letter elements.

On this premise, simple astigmats have better visual acuity, as judged by the Snellen charts, when the cylinder lies at 180 degrees than when it is at 90 degrees. In other words, the visual acuity of astigmats is better when the horizontal corneal curvature is the emmetropic curvature. This explains the surprisingly good visual acuity of many persons with high astigmatism whose cylinder lies horizontally.

A person of early presbyopic age who has simple myopic astigmatism and who does not wear any correction is better off for reading if his astigmatism is at 90 than at 180 degrees. On the other hand, if the astigmatism is of the simple hyperopic type it should be easier for the patient wearing no lenses to distinguish near reading matter when the astigmatism is at 180 than at 90 degrees.

An anastigmat with an undercorrected spherical error is likely to have erroneously prescribed for him a weak cylinder, axis 90 degrees. By the same token, in an anastigmat, if the spherical error is fully corrected and a weak cylinder wrongly prescribed, it should be better tolerated at axis 180 degrees than at 90 degrees.

The practical application of this discussion may be embodied in the following rule: When a weak cylinder in the horizontal axis is expected to be correct from retinoscopic examination but is demanded by the patient in the contradictory vertical axis, add more spherical correction and the patient will reverse his choice to the proper axis.

In case of doubt while refracting at this stage, the elimination of test letters by substitution of an astigmatic cross will avoid psychologic problems of letter recognition and will avert discrepancies of axis.

Dr. Adolph Posner made the photographs necessary for this work.

TUMOR OF THE THIRD VENTRICLE WITH RESULTING CHRONIC INTERNAL HYDROCEPHALUS

CLINICAL HISTORY OVER A PERIOD OF SEVENTEEN YEARS

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Tumors of the third ventricle which cause chronic internal hydrocephalus are not uncommon, but the case here reported is interesting clinically because of the fact that the patient was followed for seventeen years and that death was due to a traumatic subdural hemorrhage.

The symptoms of a tumor of the third ventricle depend on the size and location of the growth and the involvement, either directly or through distant effects, of the important structures surrounding the ventricle. Weisenburg's [1] paper published in 1910, in which he reported typical cases, gave a good summary of these symptoms, as they were caused either by direct pressure or after extension into the aqueduct of Sylvius by growth of the tumor ventrally. They were as follows: paralysis of associated ocular movements and of convergence upward and, less commonly, to either side or downward; ataxia of the cerebellar type, as shown by the gait; stationary or voluntary movements of the limbs; occasional ptosis of the upper eyelids and protrusion of either one or both eyeballs, and, as a rule, large pupils with impaired reactions, paresis of the limbs of one or both sides and the general symptoms of tumor, such as headaches, choked disk, nausea, vomiting and vertigo. Tumor of the third ventricle does not cause specific mental symptoms; the occurrence of such symptoms is dependent on the compression of the cortex against the skull, resulting from internal hydrocephalus.

Fulton and Bailey [2] reported a series of cases of tumor in the region of the third ventricle from Cushing's service at Harvard Medical School in 1929 and gave a further important résumé of the symptoms produced by the growths, with an extensive bibliography Other cases have

Read before the Philadelphia Neurological Society, April 28, 1939.

1. Weisenburg, T. H.: Tumours of the Third Ventricle with the Establishment of a Symptom-Complex, Brain **33**:236-260, 1910.

2. Fulton, J. F., and Bailey, P.: Tumors in the Region of the Third Ventricle: Their Diagnosis and Relation to Pathological Sleep, J. Nerv. & Ment. Dis. **69**: 1, 145 and 261, 1929.

been reported in the intervening ten years, but Dandy [3] summarized the present knowledge as follows:

There is no syndrome of the third ventricle, per se, but tumors immediately affecting this cavity may cause characteristic symptoms by pressure upon its walls, and their contained nuclei and tracts. Among the well recognized syndromes due to lesions of these structures we may mention: (1) the infundibular syndrome (polyuria, adiposity); (2) the syndrome of the central gray matter around the posterior end of the third ventricle and aqueduct of Sylvius (hypersomnia); (3) the thalamic syndrome (central pain, painful hypesthesia); (4) the extrapyramidal syndrome (bradykinesia, rigidity); (5) the decerebrate syndrome (hypertonicity, Magnus-de Kleijn reflexes); (6) the syndrome of Parinaud (paralysis of conjugate vertical movements of the eyeballs); (7) the syndrome of the body of Luys (hemichorea; vide Martin, 1927, Eward, 1891); (8) the hypopituitary syndrome (infantilism, hypotrichosis, lowered metabolism); (9) the uncinate syndrome (olfactory and gustatory symptoms; vide Herzog, 1928); etc., etc.

All of these syndromes are of as definite localizing value in cases of brain tumor as any other symptoms when they occur precociously before the onset of pressure symptoms. The infundibular syndrome and the hypersomnia associated with lesions of the central gray matter are deserving of especial emphasis since, owing to imperfect understanding of their localizing value, they are seldom given the importance which they merit in localizing tumors of the brain.

REPORT OF A CASE

E. W. I., a 10 year old white boy, was first seen by me on Dec. 28, 1920. He had been sent from school because of defective vision, headaches, lack of concentration in school, nervousness and occasional attacks of nausea and vomiting. Vision of the right eye was 5/6 (partly) and of the left eye 5/9 (partly). After correction of a compound hyperopic astigmatism, this was improved to 5/6 in the right eye and 5/7.5 in the left. There were a vertical tip of one eye, amounting to 2 prism degrees, and decided hydrocephalus, the head measuring 61.5 cm. in circumference. The boy wore a hat with a 7¾ head size.

Examination of the eyegrounds showed bilateral low grade optic neuritis, with a difference in level of 2 D. (0.66 mm.) between the head of the nerve and the surrounding retina. The child was at once referred to the family physician, Dr. Herman B. Allyn, who had examined him five years before. His notes made on May 22, 1916, when the child was 5 years old, recorded a large head and scars resulting from a forceps delivery. At the examination in 1920 Dr. Allyn found incoordination of arm and hand movements. The child was restless and uneasy and inclined to try to be funny and smart; lack of judgment was reported by his mother. He had a good memory and was good in school work, but he lacked the ability to concentrate.

He was referred to Dr. Charles H. Frazier at the University Hospital for study and roentgen examination of the skull. On Jan. 7, 1921, Dr. Frazier reported signs of increased intracranial pressure, as evidenced by the headache, vomiting and papilledema. In addition to this, he had signs of disturbed cerebellar function. There was marked ataxia in the movements of the upper extremities, together with dysmetria. In order to relieve the pressure and to prevent atrophy of the

3. Dandy, W. E., in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1932, vol. 12, p. 1.

optic nerves, Dr. Frazier advised subtemporal decompression and possibly a callosal puncture, although unfortunately the effects of the latter as a means of ventricular drainage were of comparatively short duration.

Suboccipital decompression was suggested as an alternative in the hope of relieving some of the cerebellar disturbances.

Consultation with Dr. de Schweinitz was asked, and on March 7 he confirmed the diagnosis of optic neuritis and beginning atrophy of the optic nerves. He also advised a decompression operation. Dr. Allyn agreed to this, and on April 14 Dr. Frazier did a suboccipital decompression. His notes made at the time of operation follow: "Bone was removed over both cerebellar hemispheres. The dural tension was much above normal but not extreme. There was a small collection of subdural fluid on the outer side of the left hemisphere, at which point the dura was punctured, and the fluid escaped as though under considerable pressure. After the introduction of a grooved director in the direction of the cisterna basalis, there was no escape of fluid." Dr. Frazier's conclusion was: "The absence of a large collection of the fluid in the posterior fossa and the evidently increased pressure lead one to the conclusion that the pressure must be due to internal hydrocephalus, with partial, but probably not complete, obstruction."

So far as the records show, a ventriculogram does not seem to have been made at this time.

After the operation the boy vomited frequently for three days, and there was an increase in the papilledema to 4 diopters and marked tortuosity of the retinal vessels. The neuritis slowly decreased, and as the patient's general condition had improved he was discharged from the hospital on May 21. Vision improved slowly, and the fields of vision gradually widened. Increased diplopia, however, appeared due to paresis of the right superior rectus muscle (oculomotor disturbance). Four months later the margins of the disks did not show any blurring, and the boy was able to return to school after the occipital wound healed. During the following three years he was seen frequently by me and by Drs. Frazier and Grant. Gradual deterioration of his mental condition became apparent. It became increasingly difficult to perform functional tests. The boy was impatient and resentful and at times refused to complete tests of the visual fields. In December 1924 he fell coming home from school, striking the left side of his head very hard. He complained of headache afterward and later had an attack of unconsciousness at home. There was no blurring of the nerve heads, and the fields had widened materially. The head measured 65 cm. in circumference at this time.

Several attacks of unconsciousness occurred, and in June 1925 he was readmitted to the University Hospital. The attacks were not accompanied by an aura. There were no convulsive movements, crying or other symptoms except for headaches, and they were of short duration. He was reported to be somewhat opinionated, stubborn and secretive but had kept up well in his school work. He was devoted to his mother but showed no sexual precocity or overdevelopment of the sexual organs. On June 19, 1 cc. of normal dye was introduced directly into the ventricle, a local anesthesia being used. The ventricular pressure measured 20 mm. Twenty minutes later a lumbar puncture was done, but none of the dye was recovered. Five and one-half hours after the operation urine was collected. It did not contain any dye; so there was every evidence that the ventricle, although not under great pressure, was obstructed. A roentgenogram of the skull showed the sella turcica to be slightly enlarged and the cerebral convolutions markedly atrophic. Vision in the right eye was reduced to 6/9 and in the left to 6/12.

There was optic neuritis, and vision measured at my office three months later was 5/7.5 (?) in the right eye and 5/12 in the left, the atrophy of the optic nerve being more marked in the left eye.

Later in 1925 the child began to have frequent convulsive attacks, without auras, but at no time did he froth at the mouth, bite his tongue or injure himself elsewhere During the following summer there was a constant running of clear fluid from his nose, which was found to be cerebrospinal in origin.

As the convulsive attacks became more frequent, he was admitted to the Training School at Vineland, N. J., and later was transferred to the Village for Epileptics at Skillman, N. J. (September 1936), when 25 years of age. In November 1937, during an altercation with another patient in his cottage, he either fell or was knocked down by the other patient, and his head struck the floor. He was unconscious for about ten minutes and then complained of dizziness and headache and soon became nauseated and vomited. There was no evidence of fracture of the skull, but a week later he became more confused, and the

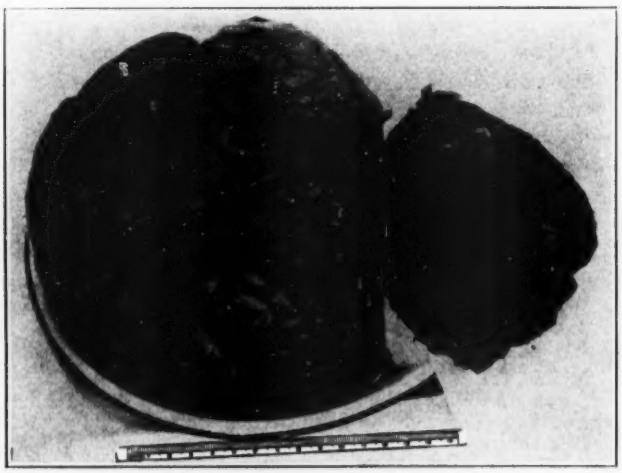

Fig. 1.—Appearance of the brain with a hematoma.

temperature rose to 104 F. as the result of a pleural pneumonitis at the base of the right lung. He was sent to the infirmary, and on December 14 respiratory distress and cyanosis suddenly developed. Acute massive pulmonary edema developed, and death occurred within two hours.

The body was sent to the University Hospital, and a complete autopsy was performed by Dr. B. J. Alpers. His report follows:

"The brain was huge, weighing 2,200 Gm. Part of the large size was the result of internal hydrocephalus, since the cerebral hemispheres were fluctuant. Most of it, however, was due to an actual increase in size of the brain, a true megalencephaly. The cerebral hemispheres were about one third larger than normal; the cerebellum and brain stem were proportionately enlarged.

Over the left cerebrum was a large subdural hematoma which covered the frontal and part of the parietal lobe. It measured 1 cm. in its thickest portion. The clot was dense and firm and appeared old; it was adherent to the overlying dura.

"The gyri were larger than normal, but there was no difference in the consistency of the gyri. They felt quite normal. Small areas of suffusions were seen over the inferior surface of the right temporal lobe. The brain in general

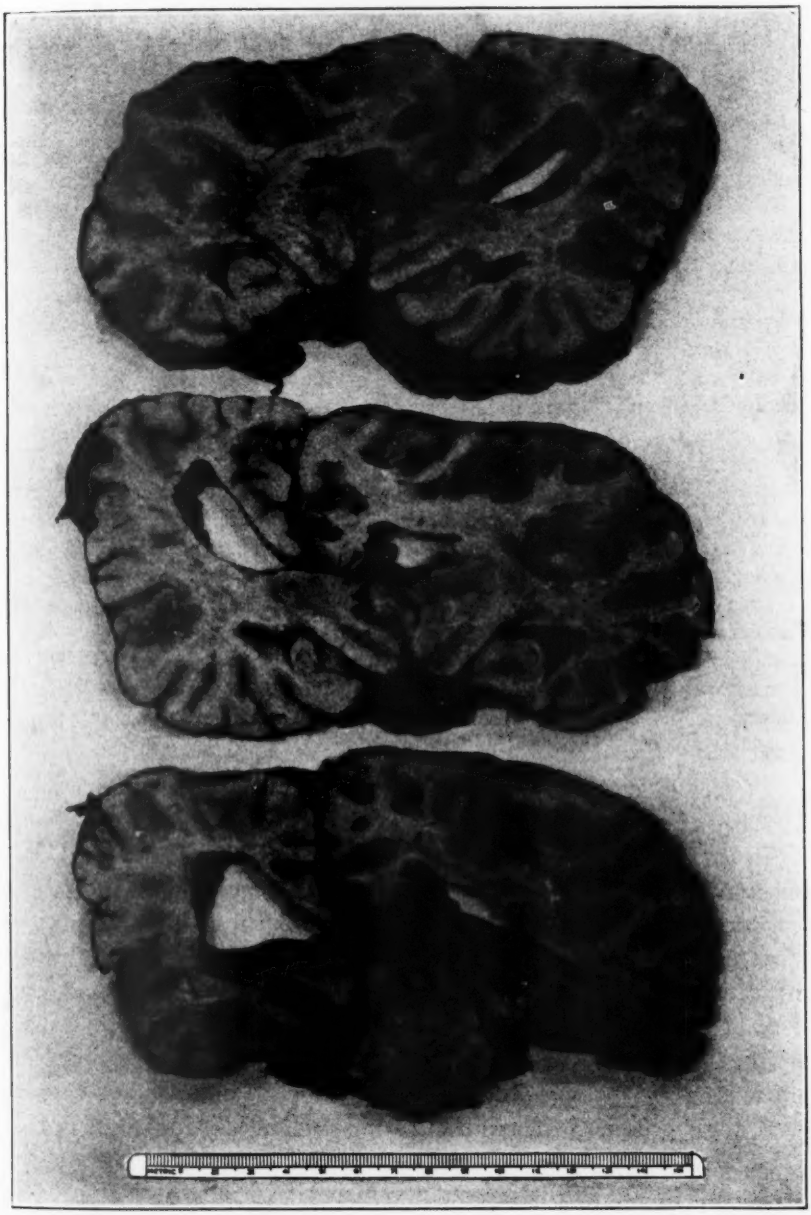

Fig. 2.—Tumor of the third ventricle, extending through the aqueduct of Sylvius into the fourth ventricle.

had a cyanotic appearance. The meninges over the base were thickened and contained blood.

"Section of the brain revealed large gyri with a large amount of white matter. Here and there, in the white matter chiefly, but also in the cortex, were small pink hemorrhagic areas. Most of these were in the left cerebral hemisphere, especially in the left frontal region. A few such areas were seen in the left putamen and several in the right parietal region. These looked like fresh areas of metastatic encephalitis.

"Filling the third ventricle was a small tumor which extended from the posterior part of the third ventricle through about the middle of the pontile portion of the fourth ventricle. This tumor was adherent to the floor of the third ventricle and to the right lateral wall of the pons. It had no relation to the pineal body. It was firmly adherent to the ependyma and seemed to arise from this structure. It did not fill the third ventricle completely, there being about 3 mm. between the top of the tumor and the tela choroidea. The tumor was white, soft and relatively avascular. Beneath it, on the left side of the mesencephalon, was a linear softening extending under the floor of the aqueduct and along the raphe to the interpeduncular space. The softening was old and contained much hemosiderin pigment.

"There was marked internal hydrocephalus involving the lateral ventricles. The ventricle behind the block (the fourth ventricle) was not dilated. The anterior horns and atrium were much more affected than the inferior horns. The corpus callosum was thin, and the basal ganglions were much compressed by the dilated ventricles."

Dr. Alpers summarized the case as one of a large brain with a tumor of the third ventricle, internal hydrocephalus, subdural hematoma and many foci of metastatic encephalitis.

The gross diagnosis was: "(1) tumor of the third ventricle; (2) subdural hematoma on the left side; (3) megalencephaly; (4) internal hydrocephalus, and (5) metastatic encephalitis."

SUMMARY

A case of chronic internal hydrocephalus in a boy 10 years of age is reported. Associated symptoms were papilledema, with failing vision and contracted visual fields, and partial oculomotor involvement. Decompression brought about relief of the intracranial pressure, with improvement of vision and widening of the fields. Gradual mental deterioration, spells of unconsciousness and later convulsive attacks occurred. There was rhinorrhea due to erosion and perforation of the cribriform plate. Death occurred at 27 years of age from extensive subdural cerebral hemorrhage due to accidental traumatism. Autopsy showed the "presence of an infiltrating tumor (astrocytoma) of the hypothalamus and the third ventricle, which extended through the aqueduct of Sylvius into the fourth ventricle, partially blocking the outflow of ventricular fluid, and metastatic hemorrhagic encephalitis of the cerebral cortex."

The surgical aspect of the case will be discussed by Dr. Francis C. Grant, who followed the case with Dr. Frazier for years, and the neurologic point of view by Dr. B. J. Alpers, who made the postmortem examination.

DISCUSSION

DR. FRANCIS C. GRANT: From the surgical standpoint, one speculation at least is of interest. The boy came under neurosurgical observation in 1921. The clinical signs were few and no positive localization of the position of the lesion producing a mild bilateral choking of the optic disks could be made. Ventriculography was not highly regarded at the time. No ventriculograms, which in all probability would have shown the position of the tumor, were made. But even if a localization could have been reached by this method, the operative approach to a tumor in the third ventricle was then, and for that matter still is, a hazardous procedure.

Could any operative attack then or now directed against an astrocytoma adherent to the floor and the ependyma of the third ventricle have assured the patient of a survival period of seventeen years? The simple, easily performed, suboccipital craniectomy, done then in ignorance for relief of pressure, accomplished an amazingly satisfactory result. Of course, the slow growth of the tumor which permitted the cerebrospinal fluid to force its way around this obstruction in the third ventricle was a fortunate circumstance. Nowadays no neurosurgeon would consider a suboccipital craniectomy for relief of pressure when the tumor was known to be in the third ventricle. Through the occipitoparietal approach, either by working through the ventricle following a transcortical incision or by mobilization or amputation of the right occipital lobe, the corpus callosum would be reached and transected and the tumor removed. With such a procedure the child would have had a 30 to 40 per cent chance of immediate death from hyperthermia or hemorrhage. If he had recovered, a marked defect of the visual field would have resulted, with possibly hemiparesis from unavoidable section of the rolandic vein. At times the valor of the modern neurosurgeon outruns his discretion. This case is important because it emphasizes the fact that a properly placed, simply performed decompression with consequent relief of pressure may produce as satisfactory results as a hazardous direct attack on the tumor.

Furthermore, in 1925, four years after operation, rhinorrhea developed. Dr. Frazier was away at the time, and the patient came under my care. No way of checking the leak seemed possible, and an attack of meningitis with fatality seemed inevitable. But within three months the rhinorrhea ceased spontaneously. Neither before nor after the leakage of spinal fluid was there any change in the clinical signs or ophthalmoscopic findings.

Convulsions then set in, and the patient was hospitalized, death finally occurring from a chronic subdural hemorrhage. If one should care to philosophize on this case, it is curiously tragic that the patient should have carried a probably inoperable tumor for seventeen years and survived a rhinorrhea which surgical intervention could not stop, only to die of a subdural hemorrhage, a lesion which is easily and safely removed by a simple surgical procedure.

DR. B. J. ALPERS: From the standpoint of pathology, I think that it is well to point out the fact that a great many of these tumors that are spoken of as tumors of the third ventricle are not really such. They are tumors which involve the adjacent brain substance and belly out

into the third ventricle. Only from that standpoint should they be spoken of as tumors of the third ventricle.

A good deal of the confusion that has resulted with regard to tumors of the third ventricle has come from regarding these infiltrating tumors which project into the third ventricle as really being tumors of the third ventricle. Actually, primary tumors of the third ventricle are rare. There are some colloid tumors which fill the third ventricle; they are really unusual. Rarely does one see dermoid cysts or other cysts arise primarily in the third ventricle. I think that if one considers the primary tumors of the third ventricle, the matter becomes simplified from the pathologic standpoint but confused from the clinical standpoint. In these cases there is a history of increased pressure and possibly of intermittent headache and, as Oldberg and Eisenhart have pointed out, a history in a small percentage of cases of personality and emotional disturbances. I do not think it is possible to make more than a good guess at a diagnosis of a tumor of the third ventricle in most instances. In cases in which there is increased intracranial pressure without localizing signs, one is entitled to a guess of tumor blocking the ventricle.

PRIMARY TUMORS OF THE OPTIC NERVE (A PHENOMENON OF RECKLINGHAUSEN'S DISEASE)

A CLINICAL AND PATHOLOGIC STUDY WITH A REPORT OF FIVE CASES AND A REVIEW OF THE LITERATURE

FREDERICK ALLISON DAVIS, M.D.
MADISON, WIS.

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INTRODUCTION AND CLASSIFICATION

Primary tumors of the optic nerve are rare. Collins and Marshall reported only 2 over a period of fifteen years among 388,000 patients treated at the Royal Ophthalmic Hospital (Moorfields) in London. Verhoeff reported that 4 primary tumors of the optic nerve were removed at the Massachusetts Charitable Eye and Ear Infirmary over a period of thirty-six years, during which time 669,557 new patients were examined. In these two large series of patients with ocular conditions the tumors occurred in the ratio of about 1 in 176,000 patients. Three hundred cases were collected from the world literature by von Hippel and were cited in the 238 references in the bibliography of this author's exhaustive monograph in the 1925 edition of Graefe and Saemisch's "Handbuch der Augenheilkunde." I have found 65 references to this subject since that date, with a report of 80 additional cases. Much confusion is still evident in this material, but considerable progress has been made in the histologic diagnosis and classification.

Since the publication in 1912 of Hudson's classic paper concerning primary tumors of the optic nerve, most authors, with the exception of those of the French school, some Spanish observers and a few others, agree that these tumors may be classified into three main types according to their histologic nature as follows: (1) those characterized by gliomatosis (glioma), which arise within the nerve stem; (2) endotheliomas, which arise in the arachnoid or the dural sheath, and (3) those characterized by fibromatosis (fibroma), which arise in the dural sheath. The tumors have been further classified according to their location in the nerve. The terms "subdural" and "extradural" have been most generally employed, since they denote the position of the growth with relation to the outer, or dural, sheath. The first two types, namely, the glioma and the endothelioma, are subdural, while the fibroma is classed as extradural, since it usually appears to grow from the outside of the dural sheath.

Verhoeff accepted this general classification but suggested the terms "intraneural" (for tumors arising in the nerve stem) and "extraneural" (for tumors arising in the sheath). He further advocated the term "glioma" in place of "gliomatosis." The former term has also been used by others.

In the cases reviewed by Hudson, as well as in those more recently tabulated by Lundberg, by far the greater number of the tumors were glial in nature, though a number of endotheliomas were also reported. Fibromatosis of the nerve sheath is exceedingly rare, few cases having been recorded.

From the Department of Ophthalmology, University of Wisconsin Medical School.

Read before the Section on Ophthalmology at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 18, 1939.

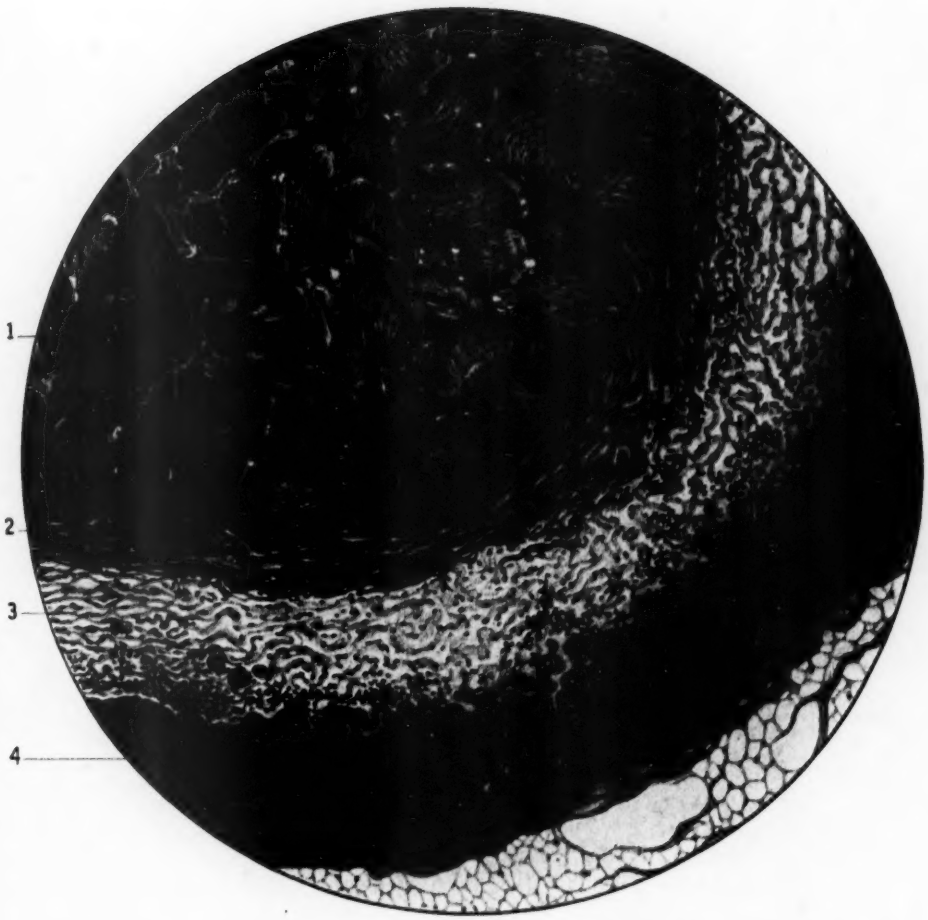

Fig. 1.—Glioma of the optic nerve in a comparatively early stage (stage *2*) of development showing: *1*, proliferation of the glia cells of the nerve stem, chiefly fibrous astrocytes; *2*, a neoplasm invading the pial sheath; *3*, hyperplasia of mesothelial cells of the subdural and subarachnoid spaces; *4*, dural sheath (thickened); Mallory's phosphotungstic acid–hematoxylin stain.

UNIV. OF MICH.

The clinical signs of tumor of the optic nerve are well known and require little comment here. The outstanding features are painless unilateral exophthalmos, which progresses slowly, accompaneid by choked disk or simple atrophy of the optic nerve, with marked reduction in visual acuity. A roentgenogram may show enlargement of the optic foramen. In the early stages the eye usually projects directly forward, with but slight limitation of motion, though this is variable. Upward rotation is usually the first to be restricted or lost. At times there is a tendency for the globe to be directed slightly downward, inward or outward, depending on the duration and the size of the growth. Ptosis may be present. Examination of the fundi may also show white spots surrounding the disk and scattered about the retina, especially toward the macula. If the choking is great, there are occasionally hemorrhages.

The diminution in visual acuity generally develops earlier in cases of glioma than in cases of endothelioma due to the involvement of the nerve stem proper in the former, while in the latter the nerve suffers later through compression.

The glioma is usually seen in the first decade of life and is probably congenital in most cases. Hudson reported that nearly 75 per cent occurred before the tenth year, though some are found in later life. The endothelioma is more frequently seen in older subjects, 50 per cent of the patients in Hudson's series being over 30 years of age. Early removal of the growth by operation is universally advised.

REVIEW OF THE LITERATURE

It is not intended in this paper to present an exhaustive review of the literature concerning tumors of the optic nerve in general, since this has been so thoroughly and ably presented by Byers, Hudson and von Hippel and more recently by Lundberg. Though some of this material has been reviewed, it would be useless repetition to enumerate all the cases cited by them.

Hudson reviewed 182 case reports up to 1912, and Lundberg tabulated an additional 123 from 1912 to 1934, making a total of 305 cases.

A summary of the pathologic diagnoses in these combined surveys reveals the following figures:

Gliomatosis (glioma)	193	(probable and certain)
Endotheliomas	86	(probable and certain)
Fibromatosis of the sheath	8	
Diagnosis uncertain	18	
	305	

Twenty-nine cases have been recorded since the publication of Lundberg's monograph. Also, there are a number of case reports in the literature not included in either of the foregoing surveys. It appears, therefore, that approximately 380 cases are on record. Reference to a

few of the more complete surveys of the subject reveals how opinions regarding the histologic structure of the growths have changed from time to time. Most of the early investigators regarded the tumors as mesoblastic in origin and designated them as fibromas, fibrosarcomas and myxomas, though there are some early cases in which a diagnosis of glioma was made.

Byers' monograph in 1902 apparently exerted considerable influence, for his conclusions concerning the histologic structure of the tumors received wide acceptance. Reference to some of the standard textbooks reveals that a number of authors still endorse his point of view. He made a complete study of the literature on the subject and tabulated 102 case reports, to which he added 2 of his own. In 1 of these cases (case 2), however, no microscopic studies were made of the original tumor, since it had been removed nine years previously, and the specimen, according to the author, was dry and unfit for study. The patient survived nine years, and on death autopsy by Adami revealed a "psammosarcoma" of the brain. In the other case (case 1), reported also by Buller in 1886, a tumor of the optic nerve had been removed from a child of 7, but a complete anatomic description of the growth was not made until fifteen years later, the specimen presumably having been in Müller's fluid during that period. For the microscopic study of sections of this tumor, the author mentioned the use of the methods of staining of Unna, Weigert, Pal-Weigert and Van Gieson. Briefly summarized, the description of the growth follows: " . . . The enlargement in the nerve was due to an increase in the intrafascicular connective tissue (endoneurium) which formed a fine honeycombed fabric, the cells of which as shown by Van Gieson and Pal-Weigert were found to be entirely free from any nerve elements proper." He also stated that the tumor of the nerve sheath was composed of "irregular flowing masses of connective tissue, which formed a meshwork of varying coarseness." He considered the growth to be primary, the tumefaction being a simple hyperplasia of all the connective tissue structures of the nerve; the sensory elements were entirely absent, and dilatation of the lymph spaces of the nerve stalk was noted.

Byers concluded from this study and his critical review of the literature that "indefinite as the term fibromatosis may be, it well defines in a general way all the changes that occur in the tumors under discussion." The tumors in 10 of 100 cases, however, in which he tabulated the anatomic diagnosis given by authors recording them, were reported as some form of glioma, gliomyxoma and gliomyxosarcoma. He considered the tumor of the nerve but a part of a neoplasm more or less widely affecting other structures within the skull.

Parsons (1905) made an extended reference to Byers' review in his textbook, "The Pathology of the Eye." In this work he stated that there is little evidence in favor of specific neuroglial proliferation in these tumors, though this occurs as a subsidiary phenomenon. He agreed with Byers that the growths are essentially of mesoblastic origin.

Hudson (1912) rejected the findings of a majority of investigators to that date and concluded that most of the primary tumors of the optic nerve arise from the neuroglia within the nerve stem. He based his conclusions on a study of 183 cases collected from the literature and 3 cases which he reported. He stressed the fact that the overgrowth of glial tissue is the essential feature of these tumors, though many authors had not recognized this. Hudson considered the growth a "degenerative gliomatosis," following the term "gliomatous degeneration" suggested in a case report by Fischer. He placed considerable emphasis on the fact that no recurrence of the new growth in the orbit had been recorded. The term "degenerative gliomatosis" implies "a generalized overgrowth of neuroglial tissue of infiltrative character dependent on some degenerative change in the tissues of unknown etiology." He remarked, however, "that in many, if not the majority, of cases it [the new growth] is not limited to the orbital portion of the nerve, but extends into the intracranial cavity more or less extensively." Hudson attributed the recognition of the real nature of the tumors to Leber and Willemer and stated that the tumor tissue is characterized by cells first described by Vossius and Salzman. He listed the tumors in 29 of the cases he reviewed, however, as true endotheliomas, with those in an additional 28 as probably endotheliomas.

Verhoeff (1922), in an extensive analysis of this subject before the American Ophthalmological Society, based on a histologic study of 11 tumors, confirmed the findings of Hudson and, as noted previously, advocated the classification "intraneural" and "extraneural." A further communication by Verhoeff (1932), in which he reported a study of 12 additional tumors, substantiated his view that "almost all, if not all of the primary intraneural tumors of the optic nerve described in the literature are gliomas."

Von Hippel (1925), in the monograph cited in the opening paragraph of this paper, concluded that most tumors of the optic nerve originate from glial tissues, though some originate from the arachnoid membrane. He suggested that there is probably an inherent growth tendency in both glial and mesodermal tissues. He considered proliferation of the glia the most important factor in this type of tumor but noted that in many cases there is also proliferation of connective tissue within the nerve sheath, which proliferation is of so great a degree that, although intermingled with the glia, it cannot be overlooked in characterizing the tumor. He doubted that it is entirely justifiable to designate such tumors as "glioma" and suggested the term "fibrogliomatosis," which indicates that proliferation of both ectodermal and connective tissue occurs.

Oberling and Nordmann (1927) offered a different and original classification of tumors of the optic nerve based on the studies of Oberling. They stated that in general the characteristic cells of most of the tumors belong to the leptomeninx, which are special cells that are distinct from

endothelial cells, which they called meningioblasts, though they described tumors arising from the glial elements of the nerve as well. These meningoblasts are presumably the normal mesothelial cells which line the subdural space. They frequently appear on the outer surface of the arachnoid membrane, grouped in clusters or nests. The neoplastic cells, according to these authors, show finely fibrillar acid-staining cytoplasm, with an oval or round nucleus containing fine granular chromatin, enclosing at times a large opaque nucleolus. The nucleolus can become transformed into a vacuole, which then occupies a large part of the nucleus. These cells vary in their arrangement, according to the authors:

> At times they are in nests like epithelial cells; again they are vaguely polyhedral and fusiform. At times they arrange themselves in whorls, in the center of which appear collagenous spheres. The structure of their cytoplasm gives them a neurogenic appearance, while their polyhedral form resembles epithelial cells; the whorls, made up of fusiform cells, resemble fibroblasts of fusiform sarcoma.

Oberling and Nordmann expressed the opinion that these meningioblasts are cells of neural origin which have wandered into the perineural mesenchyme and that they are homologous to the cells of Schwann. They therefore identified three systems of neuroglia: (1) central glia, (2) glia of the nerves formed by the cells of Schwann and (3) meningioblasts. They suggested a comprehensive classification of tumors of the optic nerve based on the neuroepithelial theory of Oberling.

Satanowsky and Androgué (1929) accepted the interpretation of Oberling and Nordmann and rejected that of von Hippel. They insisted that most of these tumors arise from the meninges, especially the arachnoid, and considered them to be meningioblastomas. They reported 6 cases, with detailed histologic descriptions.

Many other authors, particularly from the French school, followed the lead of Oberling and Nordmann and therefore adopted the term "meningioblastoma" in describing these tumors.

Lundberg (1934), in the monograph previously referred to, presented a historical review of the subject and reported 10 cases of primary tumor of the optic nerve and chiasm from the Caroline Institute of Stockholm.[1] Nine tumors were reported as gliomas of the oligodendrocytoma type and 1 as a meningiopsammoma. This is one of the most exhaustive studies of the subject that has yet appeared and should receive serious consideration of workers in this field.

The statistical data now available reveal that the tumors in nearly two thirds of the cases on record are predominantly glial in nature, while about one-third may be grouped under the classification "endothelioma."

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1. I studied some of these sections during a recent visit to the Caroline Institute, by permission of Dr. Lundberg and Professor Henschen.

That disagreement in terminology still prevails is further shown by brief reference to some of the standard textbooks.

Parsons' text (1927) retains the classification "intradural" and "extradural" tumors. He stated that "they (the former) rarely spring from true nervous tissue (gliomata–resembling cerebral gliomas) but usually originate in the connective tissue septa derived from the pia mater and from the arachnoid sheath." He regarded most of these and the extradural tumors as probably endotheliomas.

In Friedenwald's "The Pathology of the Eye" (1929) tumors of the optic nerve are divided into two groups: (1) those arising in the nerve sheath, which are designated "neurofibroma" and "neuroma," and (2) gliosarcomas of the meninges, which, according to the author, "grow down the sheath of the nerve by simple extension from the cranial cavity."

In the tenth English edition of Fuchs's "Diseases of the Eye" (E. V. L. Brown translation) it is stated:

> Primary tumors of the orbital portion of the optic nerve are predominantly of two kinds:
>
> 1. Endotheliomata, which develop from the dural sheath.
>
> 2. Those which develop from the subarachnoidal trabeculae; from the pial sheath; from the septa; from the supporting tissue of the optic nerve and, according to their histologic make-up, are called: fibroma, sarcoma, myxoma, myxosarcoma, and glioma.
>
> However, despite all this, they all belong to one form and only represent varying forms of neurofibromatosis.

Collins and Mayo in their "Pathology and Bacteriology of the Eye" (1925), van der Hoeve in Beren's "The Eye and Its Diseases" (1936), Verhoeff in Penfield's "Cytology and Cellular Pathology of the Nervous System" (1933) and Rhea in "Neuro-Ophthalmology" (1939) follow in the main the classification of Hudson.

It is evident from the literature cited that there is still some difference of opinion concerning the nature of primary tumors of the optic nerve. When one carefully studies the numerous detailed histologic descriptions which are on record, particularly those of tumor tissue for which the modern differential staining methods have been used, the tumors appear to fall in two main groups, namely, gliomas and endotheliomas (meningiomas), the former being much the more commonly encountered. The terms which have been commonly employed to designate the site of the growths, namely, "intradural" (subdural) and "extradural," as well as "intraneural" and "extraneural," appear equally unsatisfactory to me.

Both gliomas and endotheliomas are subdural (intradural) and both are also usually extraneural. A glioma starts as an intraneural growth but almost invariably later penetrates the pia and grows in the inter-

vaginal spaces, where it is no longer strictly intraneural but has become extraneural or subdural. Likewise an endothelioma may be extradural as well as intradural (subdural), depending on the seat of origin. I therefore believe that the terms should be abandoned since they are too confusing and often inaccurate.

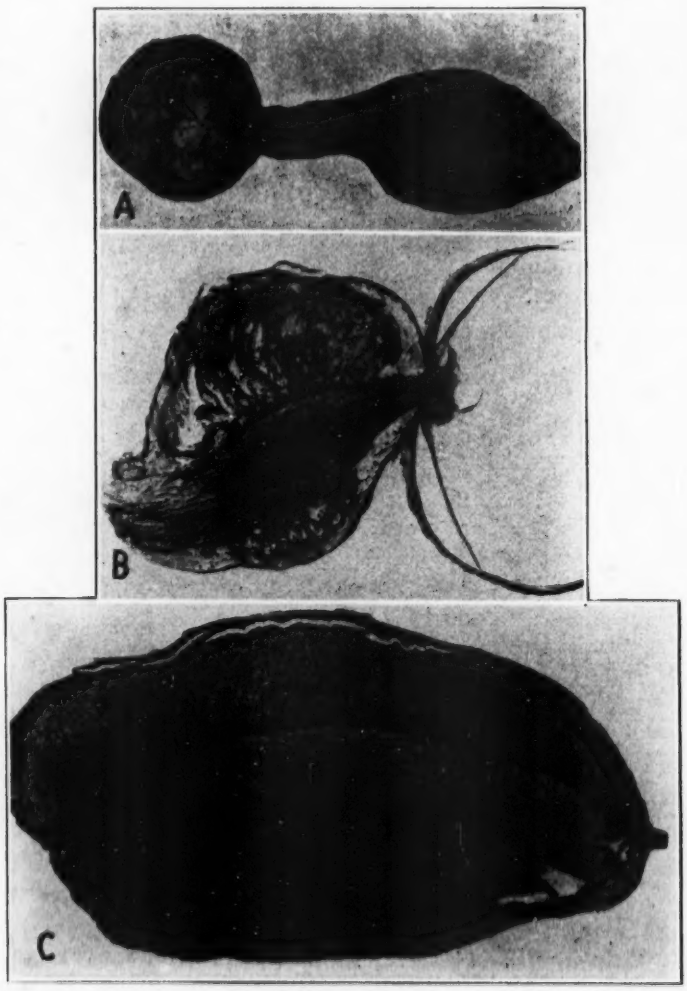

Fig. 2.—*A*, glioma of the optic nerve. *B*, glioma of the optic nerve showing cystic and gliomatous involvement of the optic disk. (*A* and *B* are from Verhoeff, F. H.: Primary Tumors of the Optic Nerve, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 3, p. 1029; Primary Intraneural Tumors of the Optic Nerve, Arch. Ophth. **51**:120, 1922.) *C*, glioma of the optic nerve. (From Reese, R. G.: Primary Intradural Tumor of the Optic Nerve, Arch. Ophth. **49**:515, 1920.)

Gliomas.—Gliomas (fig. 2) arise within the nerve stem from abnormal proliferation of the neuroglial cells. Since the nature of such tumors

and their relation to Recklinghausen's disease are the theme of this paper, a more complete description of them will be deferred until after the case reports.

Endotheliomas.—Endotheliomas (meningioma and arachnoid fibroblastoma) involve the sheath of the nerve, the nerve stem proper being affected only indirectly from the pressure (fig. 3). Histologically this type of tumor is characteristic. The general structure is entirely different from that of the glioma. As a rule the tumor is made up of masses of cells (fig. 4) resembling those of the "arachnoid clusters," or cell nests, which are normally seen on the outer aspect of the arachnoid membrane. They appear in closely packed whorls or bundles with relatively little intercellular connective tissue, though this appears at times in the septums which divide these masses of cells. The nuclei are large and oval, staining faintly with hematoxylin. Whorls of hyalinized

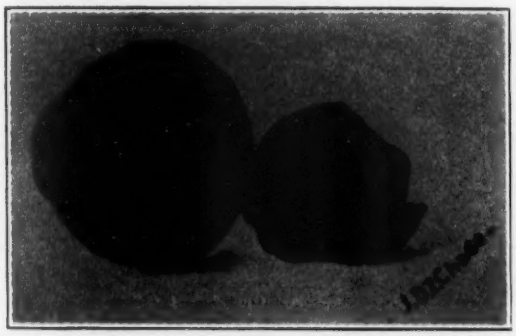

Fig. 3.—Psammoendothelioma of the optic nerve. (From de Schweinitz, G. E.: A Contribution to the Subject of Tumors of the Eyelid and Orbit [case 3], Tr. Am. Ophth. Soc. **14**:341-355, 1915.)

connective tissue, hyalinized blood vessels and corpora arenacea or psammoma bodies are frequently present. The tumor appears to spring from the arachnoid sheath as a rule, though it often invades the dural sheath of the nerve. At times it arises from the dural sheath itself (Benedict, Parker, Stephenson) (fig. 5). While it does not invade the nerve stem, it frequently spreads outward, through the dura into the orbit. It resembles an intracranial tumor of the type described as meningioma (psammoma type) by neurosurgeons and neuropathologists.

The origin of such tumors is still a controversial subject. Whether they are truly primary growths which arise within the intraorbital part of the sheath of the nerve or merely extend into it from a similar growth within the cranium is not always clear. Verhoeff emphatically stated that an endothelioma arising from the intraorbital portion of the optic nerve has not yet been demonstrated. Other writers evidently do not accept this point of view.

Unquestionably many of these tumors arise by direct extension from intracranial meningiomas, as in the case reported by Worster-Drought, Dickson and McMenemey. However, since intracranial meningeal tumors are at times multiple, there seems to be no valid reason why they should not also appear as primary growths in the arachnoid or the dural sheath of the optic nerve. The growth in a case reported by Parker and Benedict, with an autopsy report by Kernohan and Parker some years later, appears to have been of this nature. In this case

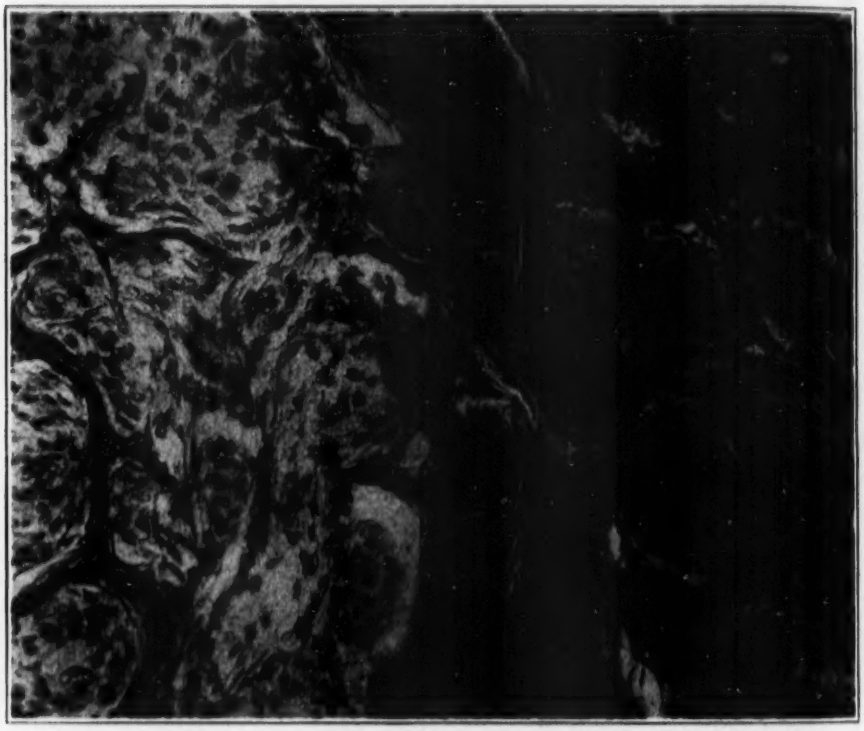

Fig. 4.—Cell nests in an endothelioma of the arachnoid sheath (arachnoid fibroma). (Photograph of a section supplied by Dr. E. L. Goar; unpublished case.)

no local recurrence appeared in the orbit after removal of the tumor, nor was there a growth found within the vicinity of the optic foramen at autopsy, although an independent growth was present elsewhere within the skull. (A more detailed report of this case is given in a later section.[1a]

It seems possible that these tumors may arise from cell nests embedded in the dural sheath of the nerve, similar to those which appear in the cranial dura, as suggested and described by Weed. I

1a. This will be found in the concluding part of this article, in the May issue, in the section on "Relations of Optic Nerve Tumors to Recklinghausen's Disease."

have on several occasions observed similar nests of cells embedded in the dural sheath of normal optic nerves.

An endothelioma of the optic nerve usually appears after the second decade of life, according to Hudson. It grows slowly and appears relatively benign. In some of the cases the patients have been followed for ten to fifteen years after operation without evidence of local recurrence in the orbit. As pointed out earlier, however, further development of similar lesions within the cranium may follow, resulting in death.

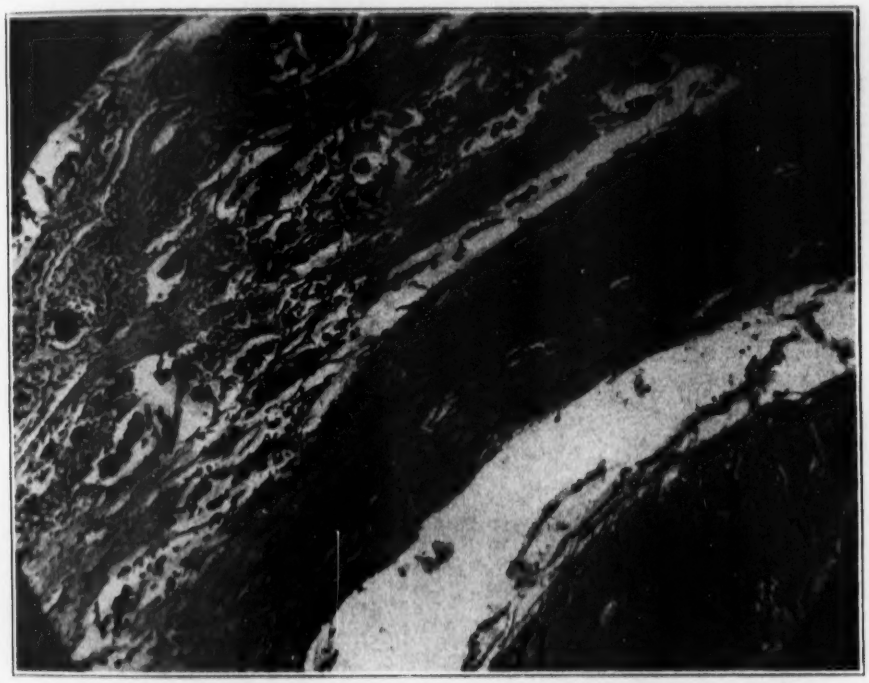

Fig 5.—Endothelioma of the optic nerve. The tumor (upper left side of illustration) arose from the dural sheath of the nerve. Note the two psammoma bodies. The nerve (lower right side) was not involved. (Photograph of a slide sent by Dr. W. L. Benedict.) Descriptions of this tumor appear in the reports of Benedict (Am. J. Ophth. **6**:182-201, 1923) and of Parker (J. Nerv. & Ment. Dis. **56**:441-452, 1922).

[Since this paper was completed, my attention has been directed to Cushing and Eisenhardt's recently published book, "Meningiomas." It contains a most illuminating chapter concerning meningiomas of the sheath of Schwalbe and a wealth of information concerning related subjects. The question of whether or not an endothelioma of the optic nerve sheath is primary in origin or merely an extension down the vaginal sheath from a similar tumor within the cranium is discussed at some length. In a postscriptum they cited several cases from the

literature—Shapland and Greenfield's (cited in a later section [1a]), Caston's and Friedenwald's (unpublished)—in which the tumors were apparently primary in origin. The authors stated that in the case of Friedenwald the proximal stump of the nerve adjacent to the foramen showed normal uninvolved nerve and nerve sheath. A roentgenogram showed a normal foramen. They concluded with the statement: "This case appears definitely to settle the debatable point we have raised."

The one example of a meningioma of the optic nerve sheath in Cushing and Eisenhardt's own series, however, arose by extension from a meningioma of the olfactory groove (fig. 6). These authors directed attention to the possibility of orbital extension by direct invasion from meningiomas which arise from various parts of the sphenoid ridge, though suprasellar tumors arising in the region of the optic foramen never seem to invade the vaginal sheath. They suggested, therefore, that the locus of origin for these tumors may be in the foramen itself and that the tumors may as well grow backward into the cranial cavity as forward down the sheath.]

Fibromatosis.—Fibromatosis of the optic nerve sheath is so rare that it has been little studied. Hudson cited but 7 cases in his review. Dr. E. L. Goar has made it possible for me to study sections from a tumor (fig. 7), the report of which is as yet unpublished. The dense connective tissue which fills the orbit is intimately fused with the dural sheath and cannot be distinguished from it. It does not involve the arachnoid, nor is the nerve invaded. Verhoeff suggested that these growths may be residual changes which follow certain inflammatory masses within the orbit. Parsons classified these tumors as fibrosarcomas of a low grade of malignancy.

REPORT OF CASES

The patients in the 5 cases herein reported have been observed over periods ranging from three months to eight years. The patients in cases 1 and 2 were brother and sister, aged 4 and 6 years, respectively. The patient in case 3 was a child of 3 years. The tumor in this case was studied at two different stages of its growth, four and one-half years elapsing between examinations. The patients in cases 4 and 5 were women aged 20 and 27, respectively. The tumors in these 2 cases involved the chiasm and the adjacent nerves within the cranium, extending into the orbital part of the nerves. All 5 patients had a mild abortive type of Recklinghausen's disease, consisting of cutaneous café au lait-pigmented patches scattered over the trunk and extremities. These associated lesions were hereditary in 4 cases, though one generation was skipped in 1 case. A child of the fifth patient had similar peripheral cutaneous changes. One patient (case 3) also had deep-seated lesions within the brain as well as other peripheral changes in the nerves of the orbit and globe, while another (case 2) had osseous changes involving

the spine and fibula. In not 1 of the cases had a diagnosis of Recklinghausen's disease been made prior to this study, though most of the patients had been repeatedly examined. The presence of the tumors was verified by operation in all 5 cases, with autopsy in 1. Histologic

Fig. 6.—*A*, endothelioma (meningioma) of the arachnoid sheath. The tumor arose by extension from a meningioma of the olfactory groove. (From Cushing, H., and Eisenhardt, L.: Meningiomas, Springfield, Ill., Charles C. Thomas, Publisher, 1938.) *B*, longitudinal section of an endothelioma of the sheath of the optic nerve. (After de Leparsonne, from Cushing, H., and Eisenhardt, L.: Meningiomas, 1938.)

studies were made of the tumors in 3 cases. A diagnosis of glioma of the optic nerve was made in all 5 instances.

CASE 1 (fig. 8).—*Diagnosis of tumor of the optic nerve; Krönlein exploration followed by enucleation and exenteration of the orbit; glial proliferation of the nerve head, glioma of the optic nerve invading the sheath, peripheral Recklinghausen's phenomena—café au lait–pigmented patches; no recurrence; period of observation, eight years.*

H. H., a girl aged 4 years, was first admitted to the Wisconsin General Hospital on Oct. 16, 1931. The chief complaint was a protrusion of the left eye of six months' duration. Examination revealed exophthalmos, the exophthalmometer reading being 15 mm. greater for the left eye than for the right. The protrusion of the eye was for the most part directly forward, with slight downward and

Fig. 7.—Fibromatosis of the dural sheath. Note the dense fibrous tissue which replaces the dura and extends outward into the surrounding tissues of the orbit. This is probably not a true tumor. Verhoeff suggested that it follows certain inflammatory masses in the orbit known as pseudotumors. Parsons referred to them as fibrosarcomas of low malignancy. Less than 15 such growths are on record in the literature. (Photograph of a section loaned by Dr. E. L. Goar; unpublished case.)

inward rotation. There was well marked ptosis. Motion of the globe was limited to downward and inward rotation. There were increased vascularity of the left upper lid and obliteration of the supraorbital fold, most marked in the outer portion of the lid. This fulness was soft and spongy, but no definite mass could be felt, nor was there a bruit. There was no bulbar or palpebral injection. The patient was unable to elevate the eye or to turn it outward. The pupil, somewhat

larger than that of the right eye, was eccentric and displaced nasally and downward. It reacted to light and dilated concentrically with atropine. Ophthalmoscopic examination showed the media to be clear. There was a definite swelling of the nerve head of about 4 diopters. The blood vessels were dilated and tortuous, with a few hemorrhages on the disk and about its margins. There was a whitish, ringlike band in the retina surrounding the disk, which was elevated. It appeared to be a low detachment or exudate under the retina. A white streak extended from this temporally and below the macula. Other scattered white spots suggesting exudate were seen in the region of the macula, and the entire temporal half of the retina appeared pale. The eye was apparently blind. A diagnosis of tumor of the optic nerve with possible extension into the globe was made.

The right eye was normal.

Previous Medical and Family History.—The child was one of twins. The previous medical history was unimportant, the child having had none of the diseases of childhood or any previous ocular trouble. The mother showed mild Recklinghausen's disease, consisting of numerous brownish café au lait patches on the skin

Fig. 8 (case 1).—*A* and *B*, front and side views of H. H. with glioma of the optic nerve. There is exophthalmos of the left eye of 15 mm. *C*, appearance of patient one year after operation (Krönlein exploration followed by enucleation and exenteration of the orbit).

of the trunk and extremities, with several soft tumor masses on the back, legs, abdomen and chest. Her face showed a number of small knoblike subcutaneous swellings, especially about the chin. Her eyes were normal. (Data were obtained after operation on the child.) The twin brother was normal, showing no ocular involvement and no other sign of Recklinghausen's disease. A younger brother, admitted to the ophthalmic ward seventeen months later, showed a gliomatous involvement of the optic nerve of one eye as well as peripheral signs of a mild type of Recklinghausen's disease.

General Examination.—The general examination was exhaustive and included a tuberculin test, a Wassermann test, a spinal puncture and neurologic study, but the results were negative aside from the presence of a number of light brown nonelevated spots scattered over the skin of the abdomen, back and legs (fig. 9). The skin over the trunk was thickened and dry. The child was under observation two months, because of an infection of the upper respiratory tract. Anteroposterior and

lateral roentgenograms and stereoroentgenograms of the skull showed no abnormal changes in the cranial bones or in the left orbit. Subsequent study of the films, however, revealed a definite change in the profile of the sella turcia. Lateral stereoscopic views showed an ovoid, pear-shaped shadow which extended from the upper anterior margin of the body of the sella turcica under the anterior clinoid process. This projection was similar to, though not as large as, that found in case 3.

Fig. 9 (case 1).—Front and back view of patient taken several years after operation. Note the café au lait–pigmented spots. These were present at birth but increased in number and became more deeply pigmented.

Roentgenograms of the optic foramens were not made before operation. Later studies were not entirely satisfactory, but there appeared to be an elongation in one axis. The foramen of the right orbit was clearly outlined and appeared normal. The skull showed no evidence of intracranial pressure.

Operation (Dec. 16, 1931).—With the patient under anesthesia produced by avertin with amylene hydrate supplemented by nitrogen monoxide, the orbit was first explored through a Krönlein incision, and an encapsulated sausage-shaped

swelling of the nerve was found. A small incision was made in the dural sheath, and a cellular soft tissue exuded. Since a malignant growth was suspected, complete exenteration of the orbit was done and the Krönlein incision sutured. Recovery was uneventful, with the usual deformity.

Macroscopic Examination.—The globe, with contents of the orbit, was photographed, but unfortunately no view was taken after the removal of the soft parts.

The tumor involved the entire nerve in varying degrees and was completely encapsulated by the dural sheath, though the latter was much thinned in places. It was somewhat spindle shaped, being smaller at either end. The globe measured 22 mm. anteroposteriorly and 21 mm. vertically and horizontally. The cornea measured 10 by 10 mm. The lens and vitreous body appeared normal. After the globe was cut a small tumor-like elevation over the disk could be seen macroscopically. The nerve, including the tumor, was much enlarged throughout its entire length, the enlargement being greatest in the posterior half. Immediately behind the globe the nerve proper measured 2 mm. in diameter and gradually increased to 5 mm., tapering again toward the apex of the orbit. The surrounding tumor increased the size considerably, the transverse measurement over all being 5 mm. at the globe and 13 mm. at its greatest diameter. The nerve was eccentrically placed within the thickest portion of the tumor mass, the distention of the subdural space being more marked on one side than on the other. It was also apparently kinked. Some portions of the nerve showed little thickening of the sheath, though the nerve stem itself was more than twice its normal size. No part of the nerve or its sheath, however, was normal, so the growth must have extended back into the intracranial part of the nerve.

The globe was severed from the nerve, a short piece remaining attached. The nerve with surrounding tumor was cut in several pieces, and it and the globe were fixed in a 10 per cent dilution of formaldehyde U. S. P. Portions were later refixed in Zenker's solution.

Microscopic Examination.—Various stains were used in preparing the sections, including hematoxylin and eosin, Van Gieson's stain, Mallory's phosphotungstic acid and hematoxylin stain, Hortega's silver carbonate stain, Cajal's gold chloride stain and Weigert's stain.

Globe: The globe appeared slightly flattened in its anteroposterior diameter. The cornea and sclera appeared normal, though the latter was slightly thicker about the posterior pole. The scleral lamellae had become separated through shrinkage. The filtration angle was free and showed no evidence of inflammatory cellular change. Schlemm's canal was present and somewhat distended. The iris presented a varied picture, depending on the area studied. In some sections it appeared fairly normal, with only a slight increase in the normal cellular content. In other sections, evidently where the pupil was drawn to one side, there was marked thickening due to an enormous increase of large branching cells with large oval nuclei. Some of the cells contained pigment and showed all the characteristics of the ordinary chromatophores. Many were nonpigmented. Masses of pigment cells were scattered through the stroma. The clump cells were broken up, the pigment spreading into the stroma. There was a beginning ectropion of the uvea. The ciliary body was shrunken but otherwise appeared normal. The choroid was thin with the exception of an area on either side of the disk, where it was definitely thicker than normal. In this area it was heavily pigmented. There was an overgrowth of fibrous elements arranged in layers, with long spindle-shaped nuclei. Blood vessels in this area were fewer than normal, though this was evident throughout the choroid. This was probably due to shrinkage from the fixation in formaldehyde.

There was a definite elevation of the disk due to marked overgrowth of glial cells (fig. 10). This swelling consisted of a reticulated and markedly vacuolated tissue in which there were no connective tissue elements but those surrounding the blood vessels. The cells branched in every direction, the processes uniting and forming a vacuolated matrix. The glial nuclei were greatly increased in numbers. Some were large and oval and deeply stained; others were more elongated and spindle shaped. This glial proliferation extended back through the lamina cribrosa into the nerve proper. It also extended into the fiber layer of the retina in a

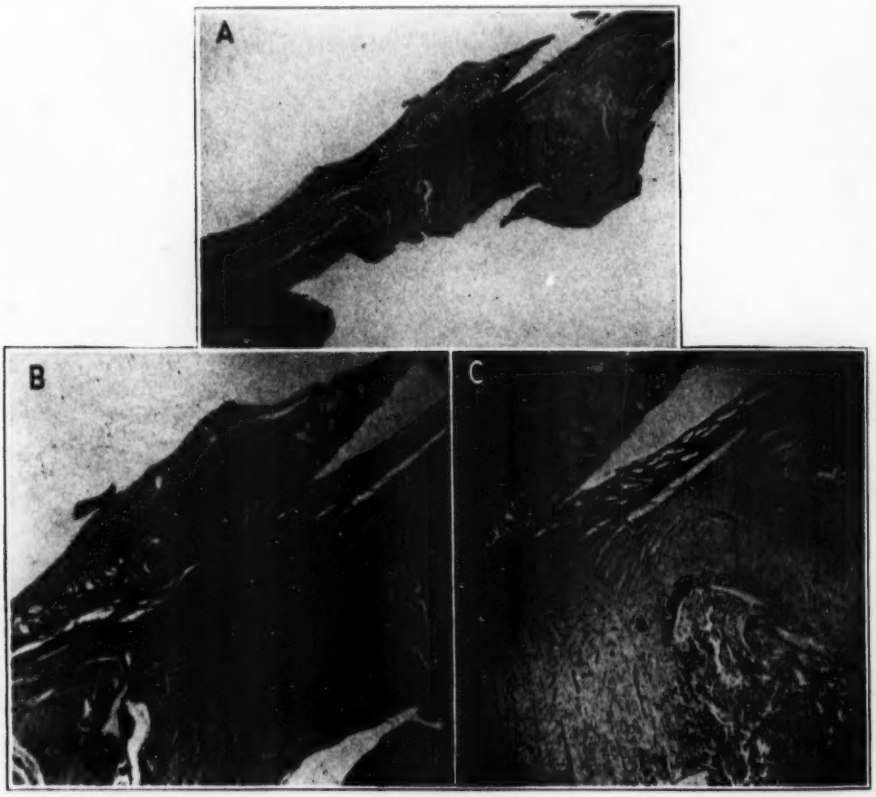

Fig. 10 (case 1).—Posterior segment of the globe. Note the glial proliferation of the nerve head, the cystic spaces in the retina and the proliferation of arachnoid cells at the anterior end of the vaginal space.

swollen area immediately surrounding the disk. The retina showed marked cystic degeneration beyond the borders of the swollen disk, the spaces being of considerable size in this location (fig. 10). For the most part they were within the nuclear layers. Farther out in the retina numerous small cystic spaces were seen situated in the outer nuclear layer as well. These cystic areas extended temporally, almost to the equator. Some contained a faintly stained transparent material and closely resembled ordinary cysts of the retina. Apparently these cysts had developed from stasis, as a result of interference with circulation brought

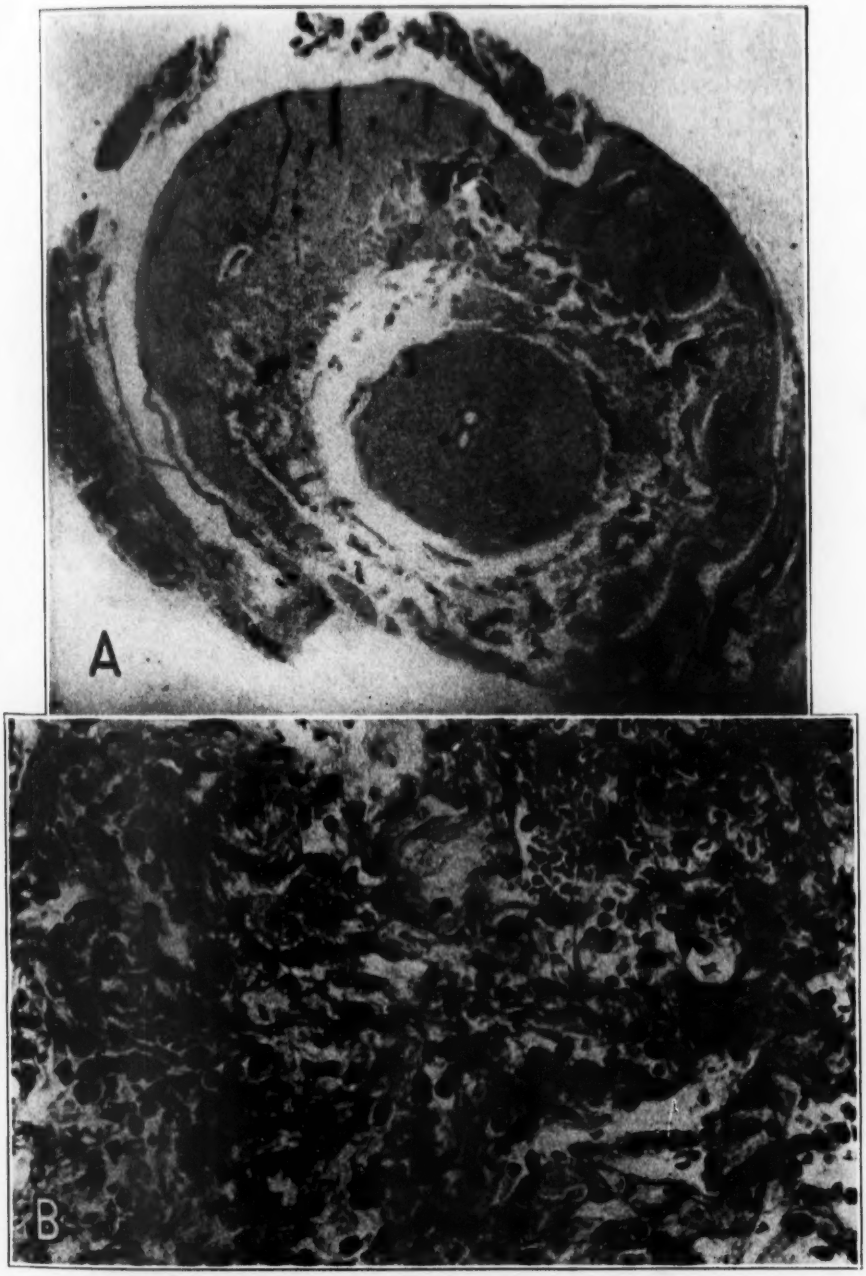

Fig. 11 (case 1).—*A*, section through the optic nerve and tumor. The section is taken near the globe. Note that the nerve stem is only moderately involved. The tumor involving the nerve sheath consists largely of proliferated arachnoid cells. *B*, arachnoid proliferation of the sheath adjoining the globe. (See figure 10.)

about by the tumor. The nerve fiber layer and ganglion cells were generally atrophic throughout the retina, with fine cystic spaces scattered through some of this area.

The lamina cribrosa was broken up by glial proliferation, though some connective tissue elements were still present. The optic nerve immediately behind the globe was of normal size, and its general appearance was fairly normal. There was, however, a definite increase in glial nuclei with some vacuoles. The pial sheath in this region was intact and of normal thickness. Outside this the subdural and arachnoid spaces were enormously distended (fig. 11 *A*) by an extremely cellular tissue, with short, oval, deeply stained nuclei which appeared much like

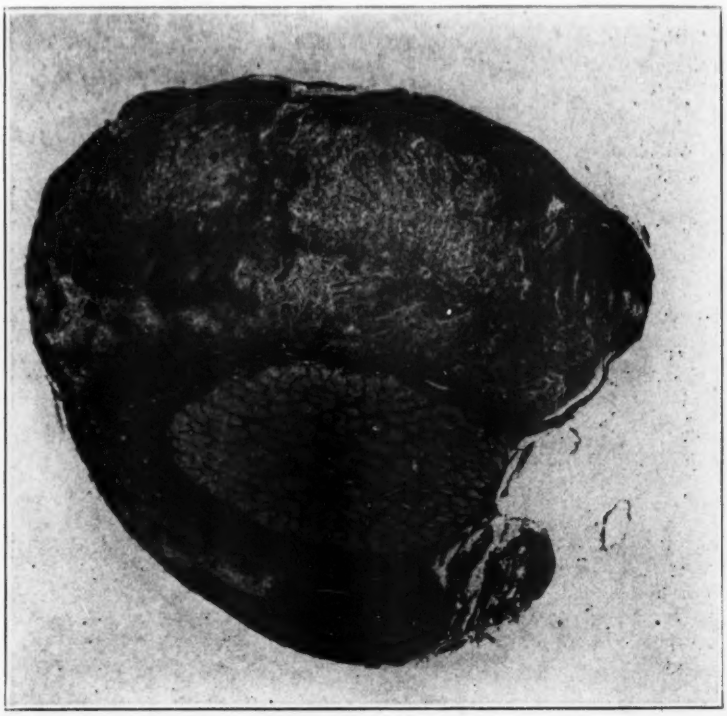

Fig. 12.—Horizontal section (oblique) of the optic nerve and tumor (stage 4). Note the large glial tumor surrounding the nerve stem.

abnormally proliferated arachnoid cells. These cells were in masses or sheets and showed no tendency to cluster formation or whorls (fig. 11 *B*). Some curled, wavy, pink-staining hyalinized bands of tissue coursed through the masses of cells, which appeared to be remnants of the arachnoid membrane. In this particular area glial fibers were not present, though transverse sections of the nerve a little farther back showed them in abundance.

Optic Nerve: The optic nerve, with the surrounding tumor, was cut transversely, and numerous sections were studied at different levels. The nerve evidently had a kink in it, since some sections were cut obliquely, while others showed double sections side by side, one being transverse and the other obliquely horizontal. Transverse sections nearest the globe showed the nerve stem within the pia to be normal in size (fig. 11 *A*). The connective tissue septums were somewhat thickened,

though their arrangement was like that of the normal nerve. The glial framework was accentuated and in most areas vacuolated. The nuclei of the glial cells were definitely increased in size and number. They were made up of large oval and round forms, the former predominating. Some were of slightly irregular oval contour. Many of the nuclei appeared in clumps, some of the cells being multinucleated. This appeared to be the result of proliferation or amitotic division. The nuclei showed a finely granular chromatin pattern, some having one large nucleolus and others two or more smaller dots. Vacuoles were especially prominent in the

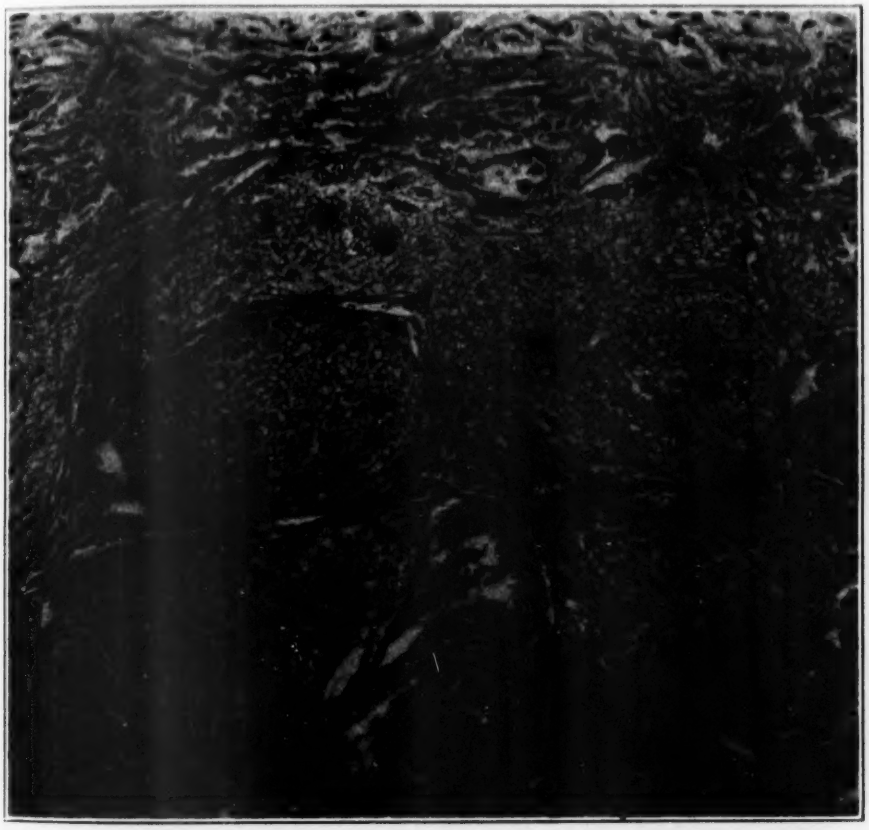

Fig. 13 (case 1).—Transverse section through the nerve stem (hematoxylin and eosin; × 200). Note the increased glial nuclei. The tumor merges with a tumor in the nerve sheath (upper portion of illustration) which it has invaded.

cell body around the nucleus, toward the periphery of the nerve. The pial sheath was present though separated and somewhat broken up in places. Outside the nerve, within the pial lamellae, glial fibers were found which extended only a short distance. Beyond this there was an enormously thickened mass of arachnoid cells which distended the subdural space, as described in the portion of the nerve attached to the globe. The dura in this region was thickened. Farther back, in the thickest portion of the specimen, transverse sections showed the nerve cut obliquely (fig. 12). It was more than twice the normal size and was surrounded by a large glial tumor

mass. The nerve here showed the usual arrangement of the funiculi, separated by connective tissue septums. The nerve bundles were increased in size. Sections which were more exactly transverse showed a honeycombed, vacuolated pattern (figs. 13 and 14), with a marked increase in glial cells. Some of the vacuoles appeared to be holes or spaces where nerve fibers had disappeared, while others were in the cell body. The nerve fibers were degenerated, the myelin sheath failing to stain except in a few places.

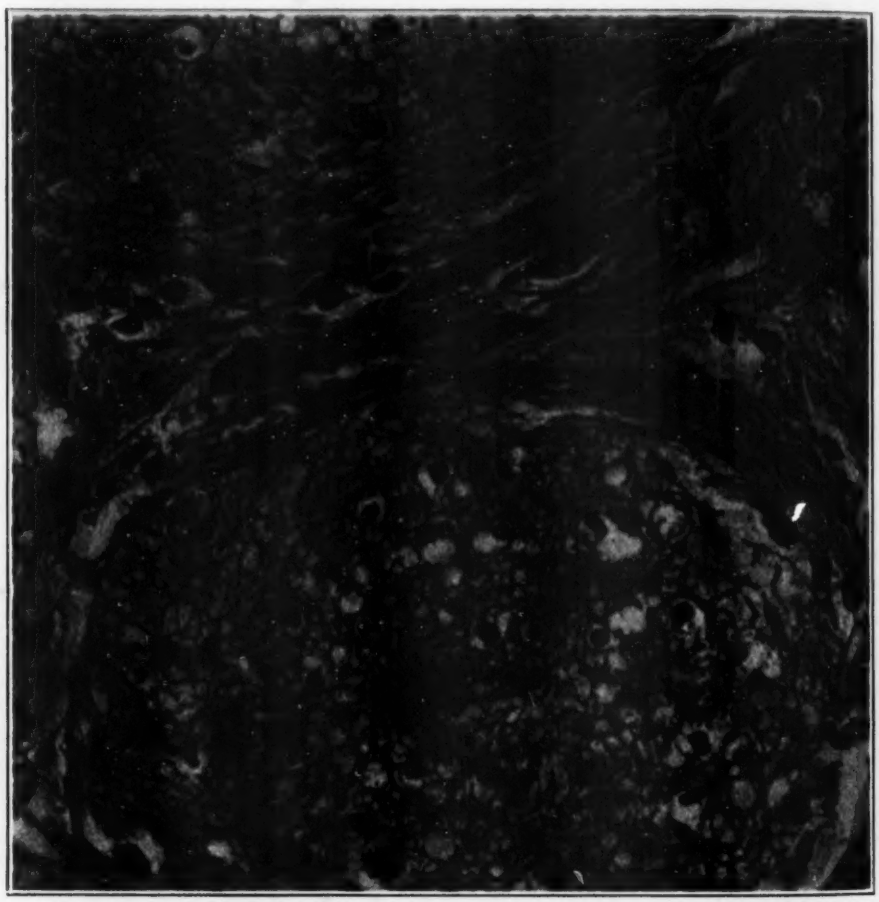

Fig. 14 (case 1).—High power magnification of the section in figure 13 (hematoxylin and eosin; × 550). Note the glial cells, chiefly astrocytes (much enlarged); the large oval nuclei, and some oligodendrocytes. Note also the condensation of glial fibers bordering the fibrous septums, vacuolation of glial cells and the holes (sites of shrunken nerve fibers).

About the borders of the funiculi, adjacent to the connective tissue septums, there was a condensation of glial fibers which in places was dense and without vacuoles. This dense mass of fibers stained deep blue with Mallory's phosphotungstic acid–hematoxylin stain. The nuclei of the cells in this region were more elongated usually than those in the central portion of the nerve fiber bundles. The

connective tissue septums were intact but in places had been invaded by glial cells and masses of fibers. The pial sheath was broken up into lamellae, in some places being unrecognizable except for a few faintly stained pink strands. Glial

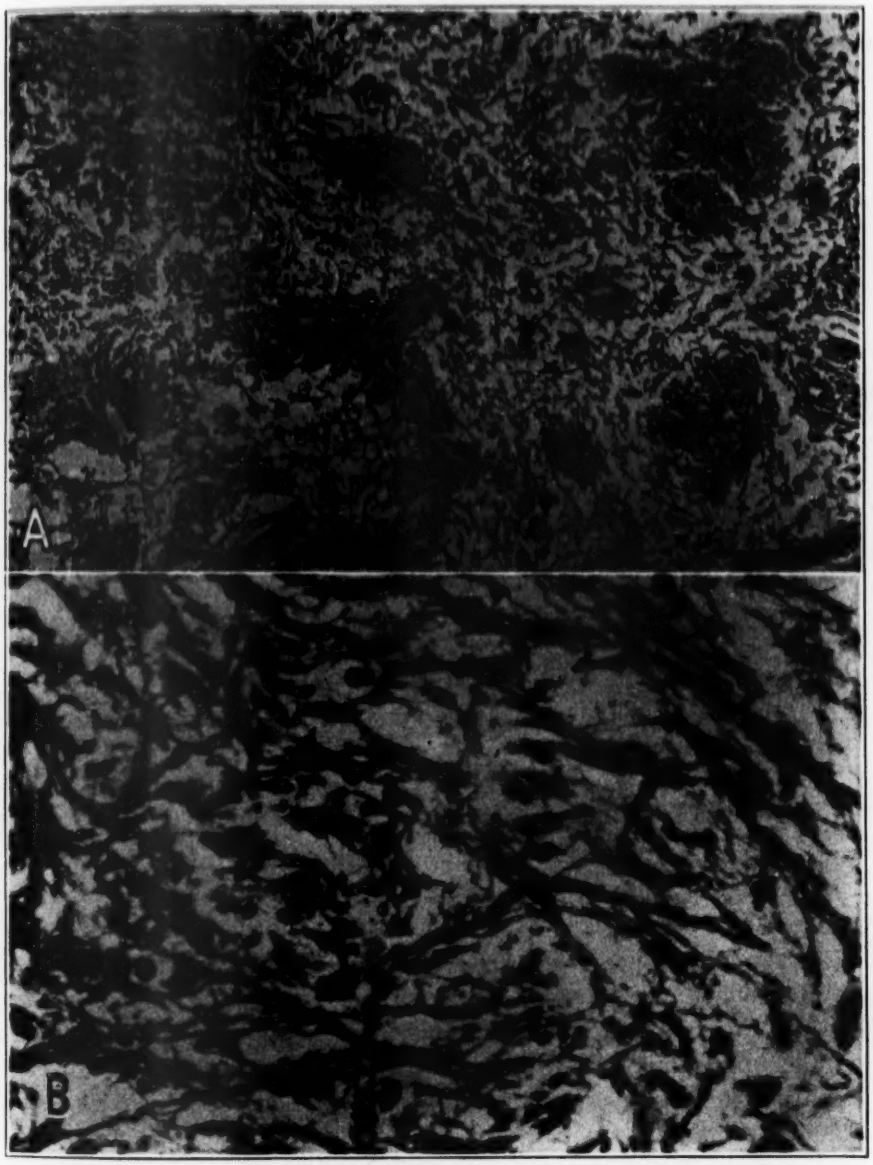

Fig. 15 (case 1).—*A*, section from the main body of the tumor in the nerve sheath—an astrocytoma (hematoxylin and eosin; × 150). Note that the only connective tissue is that surrounding blood vessels. *B*, high power magnification of a section from the tumor in the nerve sheath, showing cells with branching processes (phosphotungstic acid stain; × 400).

fibers, coarse and straight, penetrated the remains of the pia and were found in abundance throughout the tumor mass as far as the dural sheath, which they also invaded.

The tumor outside the nerve stem proper filled and distended the subdural space. It appeared to be made up largely of a reticulated mass of glial cells and fibers. The structure, however, was much more complex than that within the nerve. In some areas the growth was made up of a loosely meshed, highly vacuolated tissue (fig. 15). In some areas there were fairly large spaces, but no fluid or myxomatous material was found. The cells varied in contour, some being spindle shaped, with processes extending from one or both ends or more often branching in every direction. Small vacuoles were present within the cell body, many of them apparently fusing into larger vacuolated spaces. The tissue was more dense immediately beneath the dural sheath, where the cells in places were of a different type. These were evidently proliferating arachnoid cells. Neuroglial fibers permeated the entire tumor mass but were less abundant in the periphery. They were coarse and dense in places, with no definite cell attachments, while in other places they were finer and more wavy. They stained differentially with Mallory's phosphotungstic acid–hematoxylin stain in typical fashion, showing deep blue. Connective tissue elements were limited chiefly to isolated and broken strands of pial sheath and to that which surrounded the blood vessels. The latter were usually small and not a prominent feature of the tumor.

There was no evidence in the tissues of inflammatory involvement. No concretions or psammoma bodies were found. A few cytoid bodies were seen toward the outer border of the tumor mass near the dura. No part of the nerve studied was normal; so one would assume that the intracranial portion of the nerve was affected.

Differential staining with silver carbonate and gold chloride was unsatisfactory. Other stains, however, revealed beyond question the glial nature of the cells. Considering the marked similarity of this tumor to that in cases 2 and 3, the cells of which stained well with silver carbonate, the predominant cell type appeared to be astrocytes.

Diagnosis.—A diagnosis was made of Recklinghausen's disease of the abortive type, with glioma of the optic nerve stem (type, astrocytoma) invading the sheath.

Comment.—At the time of the original admission of the patient to the hospital little importance was attached to the pigmented spots in the skin. They were noted in the routine physical examination, but their significance was completely overlooked. The history of similar signs of Recklinghausen's disease in the mother and a younger brother was not obtained until fifteen months later, when the brother was admitted to the ophthalmic ward because of a slight unilateral exophthalmos. Similar café au lait–pigmented patches were then noted, and later more intensive study was undertaken. The family had attached no importance to the spots, the mother, when questioned, referring to them as "liver spots." The patient's twin brother was thoroughly examined and found to be normal. He was free of pigmented patches, and his vision and fundi were normal; roentgenograms showed his skull, including the optic foramens, to be normal.

An interesting feature of this case was the presence of glial proliferation of the nerve head, with large cystic spaces in the retina adjacent to the disk, similar to that noted in Verhoeff's case. This feature was recognized before operation and described clinically as a low detachment of the retina, with probable invasion of the retina by a tumor.

The section of nerve attached to the eyeball showed unusual proliferation of arachnoid cells. These diffuse masses of cells in some ways resembled the meningiotheliomatous type of meningeal tumors described by Bailey and Bucy. They did not, however, have the characteristics of the ordinary endothelioma or meningioma of the optic nerve, since no whorls or nests of cells and no psammoma bodies were present. Verhoeff discussed this feature of the tumors in the cases he reported, and in a personal communication he stated that he considered "the cell masses were merely proliferated arachnoidal cells and not a true endothelioma."

The marked thickening of the iris on one side and the thickened choroid presented an appearance suggesting early neurofibromatosis. The histologic picture, however, was by no means typical, nor were there other changes in the globe usually associated with this condition. The irregularity of the pupil, noted on clinical examination of the eye, was due to this localized thickening of the iris. It was much more advanced in case 3, in which the growth proved to be typical neurofibromatosis of the ciliary nerves in the iris.

The invasion of the nerve sheath by the tumor was much farther advanced in this case than that in case 2. The pia and arachnoid were almost completely destroyed in places. Only isolated remnants of the pia remained in some areas, while in others small masses of arachnoid cells were the only indication of the arachnoid membrane.

The dura over the thickest part of the tumor was invaded and almost destroyed by the growth in some places.

This patient has been examined at least once a year since operation, and there has been no change worthy of note. In a recent examination she appeared to be in good health. The pigmented patches in the skin had definitely increased in size, but no other peripheral changes had developed. There was no evidence of local recurrence in the orbit. Roentgenograms of the optic foramen showed some enlargement, but the reading was unsatisfactory, due, possibly, to the distortion of the orbit from the Krönlein operation or to erosion of the canal from further progress of the growth.

From the appearance of the sections of the tumor near the apex of the orbit, further growth of the tumor within the intracranial portion of the nerve is to be expected. If this is occurring, its progress must be exceedingly slow, for nearly eight years have elapsed since the operation.

Exenteration of the orbit in this case was unnecessary, as will be noted in the 2 succeeding case reports. The relatively benign nature of the tumor was unknown at the time of operation, and a malignant growth was suspected.

CASE 2.—*Diagnosis of primary tumor of the optic nerve; retrobulbar removal of the optic nerve with the tumor; preservation of the globe; glioma of the optic nerve, invading the sheath, and Recklinghausen's phenomena—cutaneous café au lait-*

Fig. 16 (case 2).—A. H., aged 4 years, with a glioma of the optic nerve (left eye). The photographs were taken one year before the patient's admission to the ophthalmic ward. Note the café au lait-pigmented spots, scoliosis, deformity of the left leg and slight widening of the left palpebral fissure.

pigmented spots, scoliosis and congenital deformity of the fibula; no recurrence; period of observation, six years (figs. 16 and 17).

A. H., aged 6 years, a brother of the patient described in case 1, was first admitted to the orthopedic department of the Wisconsin General Hospital on Oct. 16, 1931, the same day that the sister entered the ophthalmic ward. At this time, however, there was no complaint concerning his eyes, and he was admitted for a correction of a deformity of the left leg, which proved to be a congenital

absence of the fibula. There was also scoliosis of the spine. Bone grafts were made, and the child was readmitted to the hospital six months later for further grafts. He was admitted a third time on Jan. 5, 1933, and while in the hospital on this occasion he complained of pain in his left eye and stated that he could not see with it. He was then referred to the ophthalmic clinic, where a slight exophthalmos of the left eye was noted, measuring 4 mm. with the exophthalmometer (fig. 18). The eye projected directly forward, and there was a marked limitation of upward rotation. Movements in all other fields were normal. The

Fig. 17 (case 2).—Appearance of the patient five years after operation. Note the scoliosis and café au lait-pigmented patches in the skin.

pupils were equal and reacted normally to light and in accommodation. The media were clear. Examination of the fundus revealed an elevation of the disk of 2 diopters, with marked blurring of the margins of the disk. There were no hemorrhages or exudates. Vision in the right eye was 20/30 and in the left eye 20/70.

A diagnosis of tumor of the optic nerve was made and operation advised. The child was observed for two months because orthopedic work on the leg required further attention. During this time the choking of the disk increased somewhat, but there was no change in the exophthalmos. The vision decreased to 20/100. The right eye was normal.

Previous Medical and Family History.—The child was born at full term, but delivery was difficult, the mother being in labor twenty-four hours. No instruments were used. He had pneumonia at the age of 4 months. The boy had been in the orthopedic ward off and on for a year and a half for correction of a

Fig. 18 (case 2).—A. H. aged 5 years. *A* shows slight exophthalmos of the left eye (4 to 5 mm.). *B* shows the patient four months after operation. Retrobulbar removal of the entire tumor of the optic nerve was done. Note the faint line of scar along the lower orbital rim. *C* and *D* show the appearance of the eyes when the patient looked to the right and left. Note the perfect motility and position of the globe.

congenital absence of the lower end of the fibula, with talipes valgus and marked bowing of the tibia, as stated previously. The sister had a tumor of the optic

nerve, as recorded in case 1. The mother had Recklinghausen's disease in a mild form, the manifestation consisting of numerous café au lait–pigmented patches on the skin of the trunk and extremities and several soft, elevated mollusca fibrosa on the abdomen, back and arm and a number of firm, knoblike nodules embedded in the skin of the chin.

General Examination.—Aside from postural deformity produced by a congenital defect, the only general findings of interest were multiple smooth light brownish patches on the skin of the back, abdomen, thigh and buttocks, similar to those noted on the patient's sister. These were 1 to 2 cm. in diameter, were not elevated and did not blanch on pressure. All general laboratory tests gave negative results, and the Wassermann reaction was negative. Roentgenograms of the skull, including lateral, stereoscopic and anteroposterior flat views, showed the cranial bones to be thin, but there was no increase in convolutional markings and no spreading of the sutures. The sella turcica was normal in size, and the clinoid processes showed no evidence of erosion.

Operation (March 27, 1933).—Since operation on the sister of this child had revealed a tumor of the optic nerve, apparently relatively benign, I decided in this instance to remove the optic nerve through the soft tissues, thus preserving the globe. Further, I wished to avoid the deformity incident to the Krönlein operation or to evisceration.

With the patient under anesthesia produced by avertin with amylene hydrate supplemented by nitrogen monoxide, a curvilinear incision was made through the skin along the lower rim of the orbit and carried down to the bone (fig. 19). The periosteum was incised and elevated along the floor of the orbit as far back toward the apex as possible. A linear incision was then made through the periorbita, and the fat and muscles were pushed aside with narrow gauze packing. The nerve was easily isolated and was found to be uniformly enlarged throughout its entire length, being about 10 mm. in diameter. The nerve was carefully isolated and tied with chromic catgut at the apex of the orbit as far as one could reach. It was similarly tied near the attachment to the globe and then excised. The wound was closed, deep catgut sutures being used in the periosteum and silk sutures in the skin.

Postoperative healing was attended by considerable reaction, with swelling of the lids and proptosis of the globe. A neurotrophic opacity developed in the lower central part of the cornea on the eighth day but healed without breaking down, though a permanent light nebula of the cornea remained. The cornea was anesthetic, and it had to be protected for some time to prevent drying. The general reaction and exophthalmos finally completely subsided, with return of full motility of the globe and luster to the cornea. The eyes remained perfectly straight until recently, when a slight divergent squint was noticed. There was no exophthalmos or enophthalmos. The left pupil remained dilated to about 5 mm. The corneal anesthesia has persisted. The palpebral fissure remained slightly wider than that of the right eye.

Examination of the Fundus (postoperative, on the operating table).—The fundus of the eye was examined at the end of the operation, and an increased congestion of the nerve head was the only change that could be noted. A note on the sixth postoperative day stated that the pupil was semidilated and fixed; the fundus was as described postoperatively; the vessels were full and of normal caliber; and the color of the nerve head had not changed.

Two years after the operation (Feb. 8, 1935) the boy returned for observation, at which time the following notes were made: Vision was 20/20 in the right eye

and nil in the left eye. The right eye was normal. The position of the left eye was normal, with slight widening of the palpebral fissure. The extraocular movements of this eye were normal. There was a slight limitation of the levator muscle. The cornea showed infiltration of stroma on the temporal side just below the center, which extended to the limbus; this was faint, however, and scarcely noticeable. The anterior chamber was of normal depth. The pupil was slightly larger than that of the fellow eye; it dilated with atropine but did not react to light. The media were clear. The disk showed total atrophy of the nerve, with sharp borders. The vessels were slightly constricted, though they contained blood. The light streak was poorly seen in both arteries and veins. It was definitely present in the larger vessels near the disk but was less distinct in the remainder

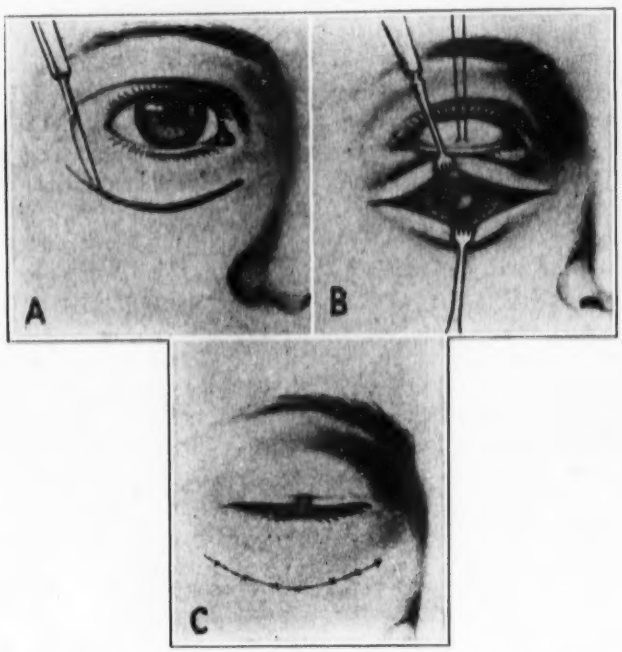

Fig. 19.—Operative procedure used for retrobulbar removal of a tumor with preservation of the globe. An incision is made through the skin along the lower margin of the orbit, as in *A*. The enlarged optic nerve is exposed, as in *B*. The nerve is tied off at the globe and the apex of the orbit, after which it is excised. The inferior rectus muscle may be detached and resutured, but no detachment of muscles was used in cases 2 or 3. The lid is sutured to prevent possible damage to the cornea, as in *C*. The wound in the skin is closed with silk sutures.

of the vessels in the periphery. There were no hemorrhages or exudates and no pigmentation.

Three and one-half years after operation (Aug. 6, 1936) the boy was again seen, and the following observations were recorded: The left eye was quiet and white. The position of the eye was good (fig. 18 *B*, *C* and *D*). The extraocular movements were normal and free in all fields. There was a slight divergence of

5 degrees. Convergence power was present but poor. The cornea showed a faint nebula 1.5 mm. wide, irregular in outline and extending across the inferior half of the cornea from the temporal side a little beyond the center. The pupil was about 5 mm. in diameter. There was anesthesia of the cornea. The media were clear. The nerve head was oval and perfectly flat and white, and the margins were sharply defined. The vessels were slightly smaller than normal; the arteries were filled. Some pigmentary changes were seen in the periphery of the fundus. Examination on Aug. 15, 1938, showed the left palpebral fissure to be slightly more narrow than the right. The left globe was slightly less prominent than the fellow eye. There was a divergence of 5 degrees. The motility was perfect in all directions of gaze. The cornea was smooth and glistening, with a faint nebula extending horizontally across it from the temporal border to the midline. The remainder of the cornea was clear. The pupil dilated well with homatropine hydrobromide; the media were clear, and the

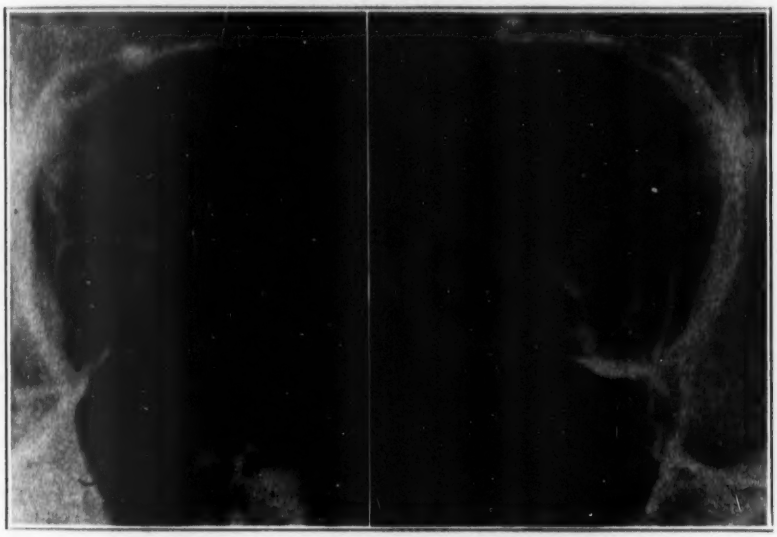

Fig. 20 (case 2).—Roentgenograms of the optic foramens (actual size). Both foramens are slightly enlarged, and the left is bean shaped.

crystalline lens and vitreous appeared normal. The disk was oval, flat and white, and the margins were sharply defined. The larger vessels showed a slight reflex as they left the disk, more definite in the arteries, and the light streak was soon lost as the vessels advanced toward the periphery of the fundus. The fundus had a normal reddish glow, and there was no abnormal pigmentation except for a few spots far out in the periphery. A photograph of the fundus showed no change from that taken two years earlier.

The right eye appeared normal; the fields and blindspots were normal.

A report of roentgen examinations follows: The skull appeared to be within normal limits; the sella turcica was normal in contour. The optic foramens measured: 5 by 5 mm., the left being slightly bean shaped (fig. 20). Further study of the films (lateral stereoscopic views), however, revealed a thin necklike shadow extending under the anterior clinoid process from the upper anterior edge

of the body of the sella turcica. This shadow was not so definite as those observed in cases 1 and 3. It was not present in the original films, taken five years earlier.[2]

Macroscopic Examination.—The excised portion of the nerve surrounded by the tumor measured 24 mm. in length. It was slightly oval, measuring 8 by 9 mm. (fixed specimen) in its thickest portion and tapering slightly toward each end, being 4 mm. at the globe and 5 mm. at the apex of the orbit. The dural sheath was intact throughout the length of the nerve. It was perfectly smooth, without adhesions to surrounding structures. The nerve stem within the pia was enlarged and was surrounded by a subdural tumor mass which was slightly thicker on one side. The thicker side measured 2 mm.; the thinner, 1 mm. The nerve stem proper, without the tumor in the sheath, measured 5 by 7 mm. in the thickest portion.

Microscopic Examination.—The nerve, cut into pieces, was fixed in a 10 per cent dilution of formaldehyde U. S. P. and in Zenker's solution and embedded in paraffin. Transverse sections were made at different levels throughout its entire length. The sections were stained wtih hematoxylin and eosin, van Gieson's stain, Mallory's phosphotungstic acid–hematoxylin stain, Hortega's silver carbonate stain for astrocytes and oligodendrocytes, the Weil-Davenport ammoniacal silver stain, Weigert's stain, Weil's iron hematoxylin and others.

Sections of the tumor showed considerable variations, depending on the level at which the specimen was cut. Sections from the thickest portion of the tumor revealed a fairly definite pattern (fig. 21). The nerve stem was much enlarged due to abnormal proliferation of the glial elements. A fairly thick tumor mass surrounded it, which was also glial in nature. It apparently arose from the tumor cells within the nerve which had invaded the pia and extended into the subarachnoid space. Surrounding this was the arachnoid sheath, much thickened, the outer cells of which showed marked proliferation. Surrounding all was the dural sheath.

Thus the tumor mass might be roughly divided into five layers or zones: first, the tumor of the nerve stem; second, the pial sheath broken up and invaded by glial cells and fibers; third, the tumor in the nerve sheath, gliomatous in nature; fourth, the arachnoid sheath, much thickened from proliferation of the arachnoid cells, and, fifth, the dural sheath.

Detailed Study of Transverse Sections: The nerve stem was more than three times its normal size. The arrangement of the funiculi, or bundles of nerve fibers, was preserved as in the normal nerve, though the bundles were considerably enlarged. The fibrous framework, or septums, showed the usual normal arrangement, but they were thickened and, in places, somewhat distended. The septums throughout the nerve were clearly demarcated, but there was no active proliferation of connective tissue cells in the septal wall. Small blood vessels

2. Since this paper was written, the patient has returned for examination. Definite evidence of an early glioma of the right optic nerve has developed since the last study (one year ago), consisting of slight exophthalmos, early choking of the disk and reduced vision. There is no evidence of recurrence of the growth in the left orbit. There are also signs of intracranial involvement. This indicates the lesions are probably multiple and that the present condition represents a further development of areas of abnormal glial proliferation in the right optic nerve and in the brain and is not necessarily an extension from the original tumor in the left nerve.

and, in places, some loosely arranged cells with oval nuclei were found within the intraseptal spaces, and glial fibers (stained blue with phosphotungstic acid stain) were also encountered within some of these spaces. The funiculi were transformed into a meshwork of honeycombed spaces, studded with innumerable glial cells (fig. 22). The honeycombed spaces were of irregular size, some of which appeared to be empty holes, the site of nerve fibers which had either disappeared or shrunk. The meshwork was evidently the glial framework, somewhat thickened and therefore more prominent. Some of these holes may have been due to shrinkage from the fixation or embedding in paraffin. (Similar holes are frequently seen to a less degree in otherwise normal nerves, and I have often observed them in degenerating nerves.) Many of these spaces, however, were vacuoles in the glial cells. With hematoxylin and eosin and Van Gieson's stain

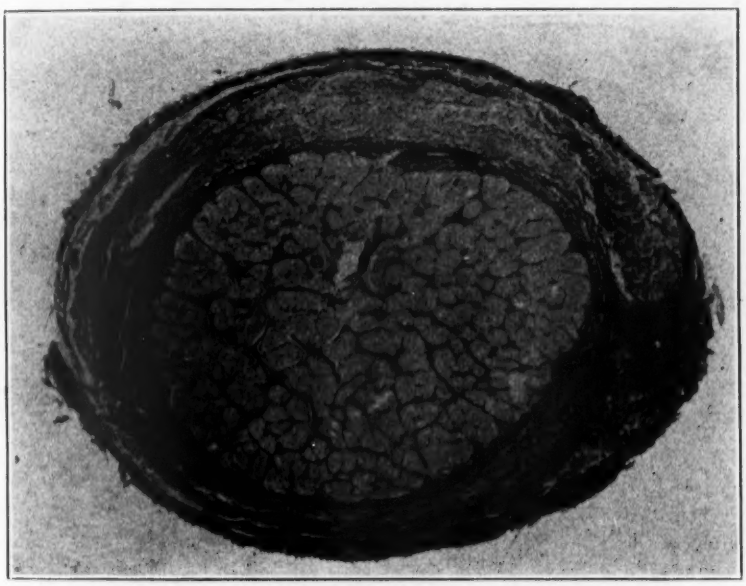

Fig. 21 (case 2).—Glioma of the optic nerve. Transverse section of the nerve and the surrounding tumor (stage 3; about $\times 20$). The nerve stem is much enlarged. The glial tumor has penetrated the pia and involves the sheath as well as the nerve stem. Note the thin layer of arachnoid cells just beneath the dural sheath.

the vacuoles were seen adjoining the nuclei. With silver impregnations the cell body was often clearly outlined, but vacuoles did not always appear definitely within them. The nuclei of the glial cells were seen most clearly with hematoxylin and eosin and Van Gieson's stain. They appeared to be of two principal varieties, large oval and round forms. Some were smaller and round. In places irregularly shaped oval forms were seen. Chromatin figures were fairly prominent, and one or two large dots were found in some of the nuclei. The nuclei were more irregular in shape and much larger than those of the normal nerve, which they otherwise resembled (fig. 23). They were especially hyperchromatic at either end of the nerve, where glial proliferation appeared in an early stage, while fiber formation was not so advanced. Multinucleated cells were frequently seen, grouped in masses, but no mitotic figures were found. The cell bodies were

so distinct and fibrous expansions so numerous and coarse that they were clearly brought out with phosphotungstic acid stains (fig. 24 *A*). With Hortega's silver carbonate stain for astrocytes and oligodendrocytes and the Weil-Davenport ammoniacal silver stain they were well impregnated and could therefore be identified as astrocytes and oligodendrocytes.

By these staining methods most of the cells which were scattered through the funiculi were found to be astrocytes. They had large oval translucent nuclei.

Fig. 22 (case 2).—Transverse section through the nerve stem and the main body of the tumor (hematoxylin and eosin; × 200). Note the marked increase in glial cells with condensation of glial fibers bordering the fibrous septums.

Each nucleus was surrounded by a cell body, irregular in shape, the cytoplasm of which appeared granular (figs. 25, 26, 27 and 28). Extending out from this irregularly shaped cell body were numerous processes branching in every direction. These were dense, coarse and wavy and could be followed for long distances. These astrocytes were of the fibrillary type. Masses of cells, often arranged in rows, were seen, with long dense fibers streaming in every direction. Frequently, however, they assumed a parallel arrangement, especially when passing

from one funiculus to another (figs. 27 and 28). Where a funiculus was completely surrounded by fibrous septums, the glial fibers collected in a concentric, laminated, feltlike layer bordering the septums. Here the nuclei of the glial cells became more elongated and lost the typical shape which they assumed in the more loosely honeycombed network of the central part (figs. 22 and 23).

Oligodendrocytes of fairly typical contour were scattered about in the funiculi (figs. 29 and 30). They usually had a round or slightly oval nucleus, which was

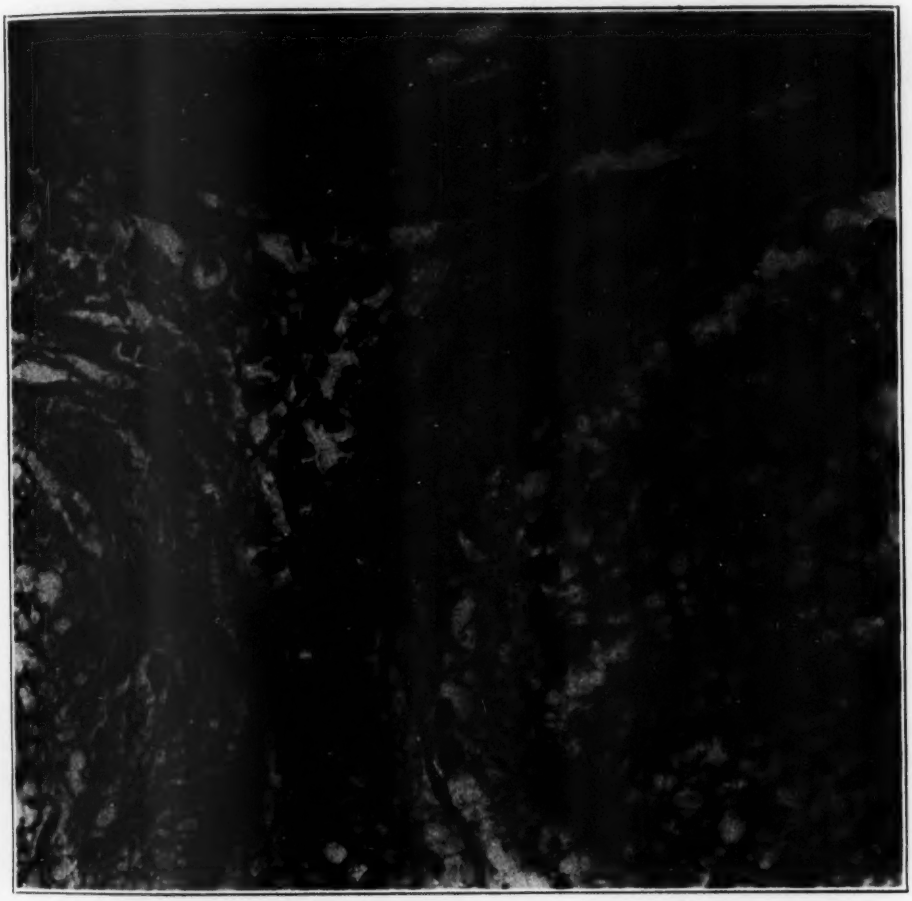

Fig. 23 (case 2).—High power magnification of the section in figure 22 (hematoxylin and eosin; × 550). Note the vacuoles in glial cells and the holes (sites of atrophied nerve fibers) and also the dense masses of glial fibers bordering the septums.

often translucent, with a small cell body containing densely impregnated granules. Short curly processes were seen extending out from the cell body for a short distance.

Subseptal attachments were clearly brought out by special stains, some of the processes being quite coarse (fig. 26). These could be seen extending from rows of astrocytes which bordered the felted bands of glial fibers. These subseptal feet

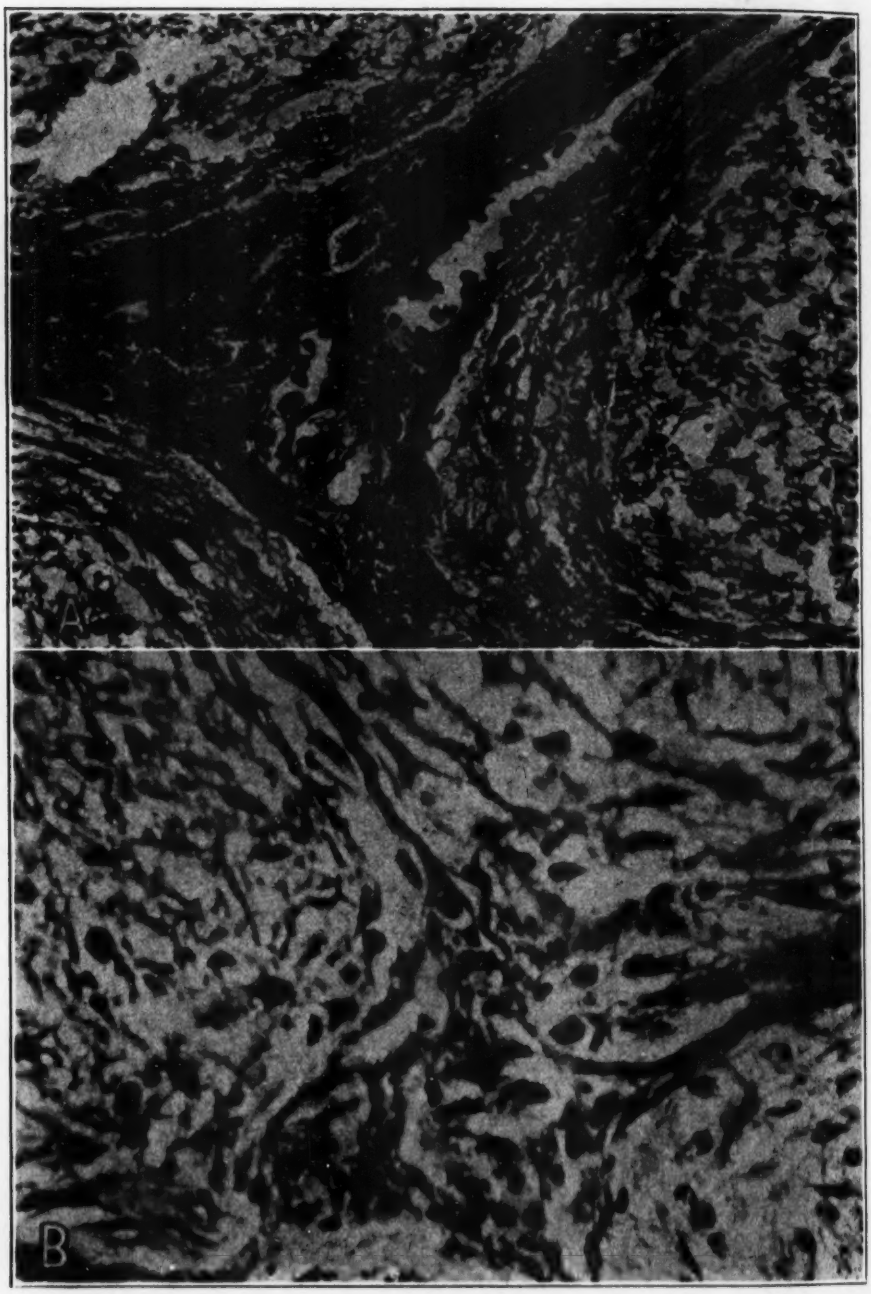

Fig. 24 (case 2).—*A*, high power magnification of the section in figure 22 (phosphotungstic acid stain; × 400). Three funiculi are seen abutting a fibrous septal space. Note the branching process of cells. *B*, same section as in *A* (hematoxylin and eosin; × 500).

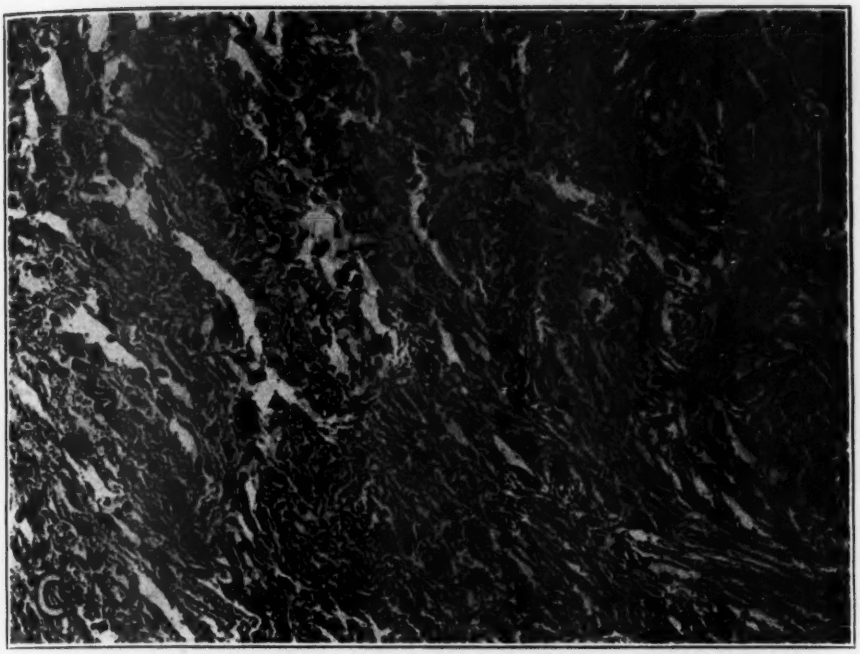

Fig. 24 (case 2).—*C*, detail of the tumor of the nerve sheath in another area; × 200. Note the coarse glial fibers and cytoid bodies. (From the section shown in figure 21.)

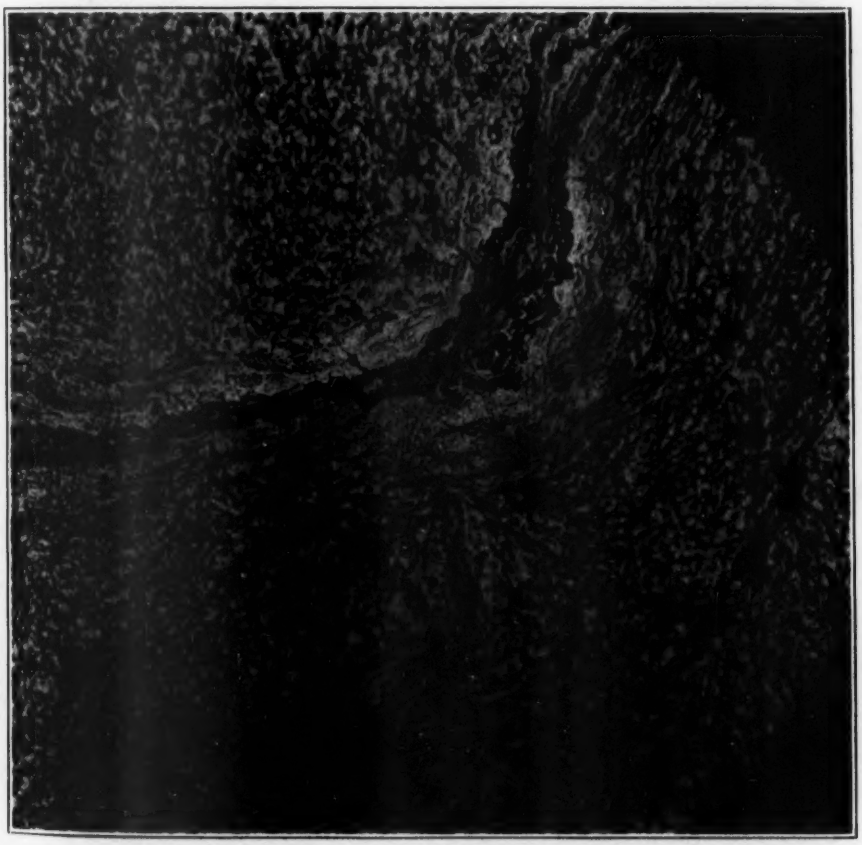

Fig. 25 (case 2).—Section from the tumor (Weil-Davenport stain; × 400). Fibrous septums are seen surrounded by dense glial fibers. Note the astrocytes.

extended at right angles through the felted glial masses to reach the fibrous septums. Subpial attachments were not so definite, though they were seen at times. The condensation of glial fibers (figs. 22, 23, 25 and 26) bordering the connective tissue septums was a striking feature of sections from the nerve in this case as well as in cases 1 and 3. These felted bands, which were composed of masses of glial fibers, were not so definite about the funiculi which abutted the pial sheath. They were present in some places to a slight degree, but they

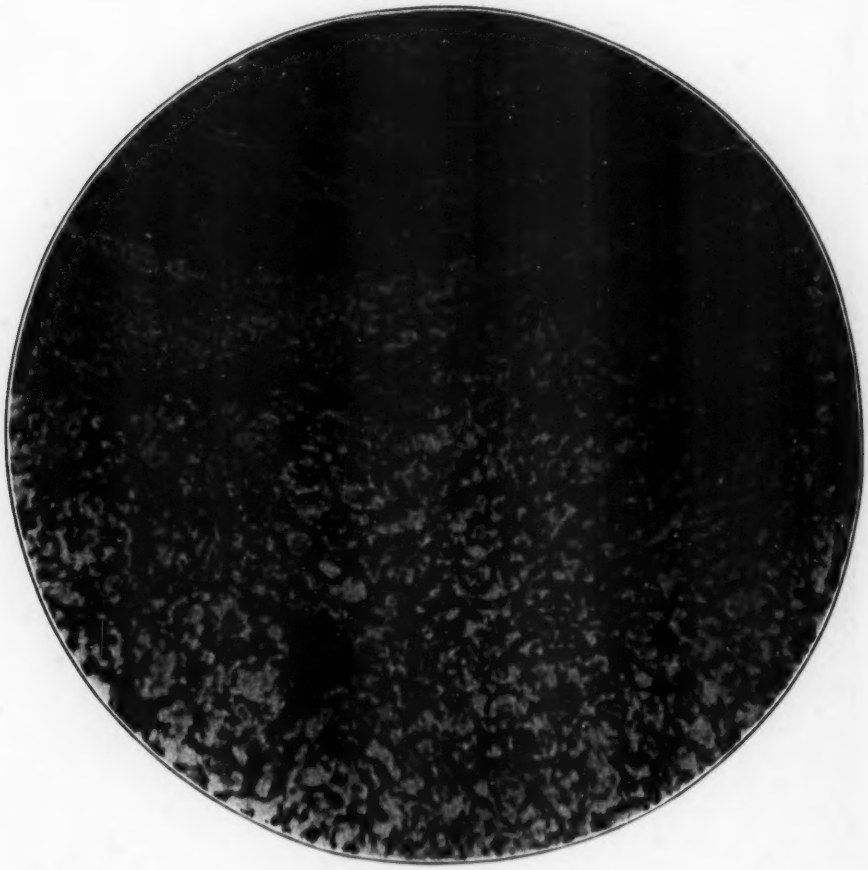

Fig. 26 (case 2).—High power magnification of section shown in figure 25. Note the large fibrous astrocytes bordering septums and subseptal expansions.

were conspicuously absent in most areas (fig. 31). Apparently the glial fibers had penetrated the pia in many places; so this particular arrangement or formation was lacking. Myelin sheaths were present in some places, but in most areas they failed to stain.

After the glial fibers left the nerve stem by penetration of the pial sheath in innumerable places, they encircled the nerve in transverse sections, running between and breaking up the pia into lamellae. The fibers appeared coarser and more dense when they were viewed in transverse sections (fig. 31).

Remnants of the pial sheath were present in most sections, but frequently they consisted only of isolated strands of pink-stained, wavy, hyalin-like tissue, embedded in glial fibers, which stood out in sharp contrast since they stained deep blue. Where the tumor was not so far advanced, the pial sheath area was much wider, though the lamellae were separated and distended by gliomatous tissue.

The glial cells and fibers extended out beyond the pial zone, where they formed the main body of the tumor of the sheath, distending the subarachnoid space (fig. 32). The tumor here consisted of a reticulated mass of tissue, fairly dense in

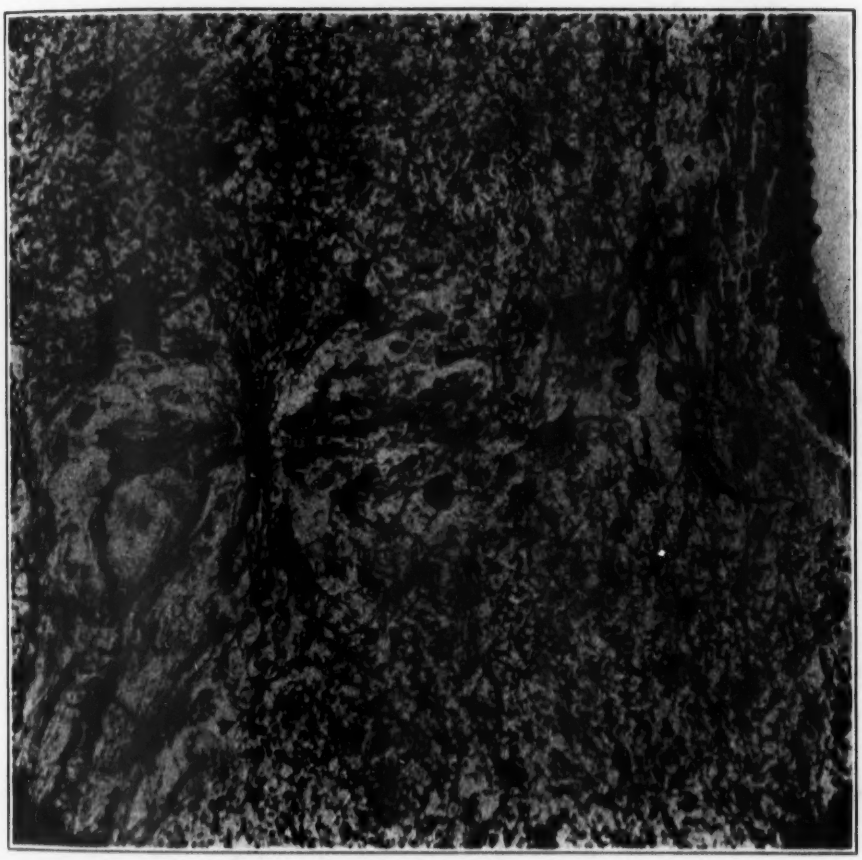

Fig. 27 (case 2).—Section from the tumor in the nerve stem (silver stain; × 400). Note the neoplastic astrocytes with thick, coarse processes.

places and more loosely arranged in others. Many vacuoles and larger spaces were present. The vacuoles were in the cell body, while the larger spaces appeared to arise from a breaking down or fusion of the vacuoles. No myxomatous material was found in these spaces. The cell bodies were more spindle shaped in this region, long processes extending from each end (similar to fig. 15 *B*). They resembled the cells of the densely felted areas of the nerve stem. Typical star-shaped cells, however, were occasionally seen, with coarse wavy processes extending in every direction. The cells apparently communicated with each other

in some areas and therefore might be described as a "coarsely reticulated syncytium." The outer aspect of the gliomatous mass of tissue was bordered by the arachnoid sheath and the dura.

The arachnoid consisted of hyalin-like, wavy, strands of tissue, staining deep pink (phosphotungstic acid), embedded in and on the outer surface of which were masses of proliferating arachnoid cells. This area also differed from that in case 1 in that the glial cells and fibers had not penetrated or invaded it to such a marked degree. Outside this thickened arachnoid the dura was present throughout

Fig. 28 (case 2).—Section of the same tumor as shown in figure 27. Note the astrocytes and oligodendrocytes.

the tumor. It was fairly normal in appearance, though somewhat thinned in places. Glial cells or fibers invaded it except in a few limited areas.

Small blood vessels appeared throughout the part of the tumor which invaded the nerve sheath, though they were not numerous.

A few cytoid bodies were found in the gliomatous mass invading the sheath. They stained a deep pink and were somewhat elongated and club shaped. With phosphotungstic acid, however, they stained a deep blue-black. Connective tissue elements were conspicuously absent throughout the tumor, except that surrounding the blood vessels and that which made up thickened arachnoid and the remnants of the pia.

Diagnosis.—A diagnosis was made of Recklinghausen's disease of the abortive type, with glioma of the optic nerve (type, astrocytoma) invading the sheath.

Comment.—The previous study of the sister of this patient and the microscopic examination of the tumor of the optic nerve which was removed made the diagnosis relatively simple in this case. Retrobulbar removal of the tumor with preservation of the globe was therefore

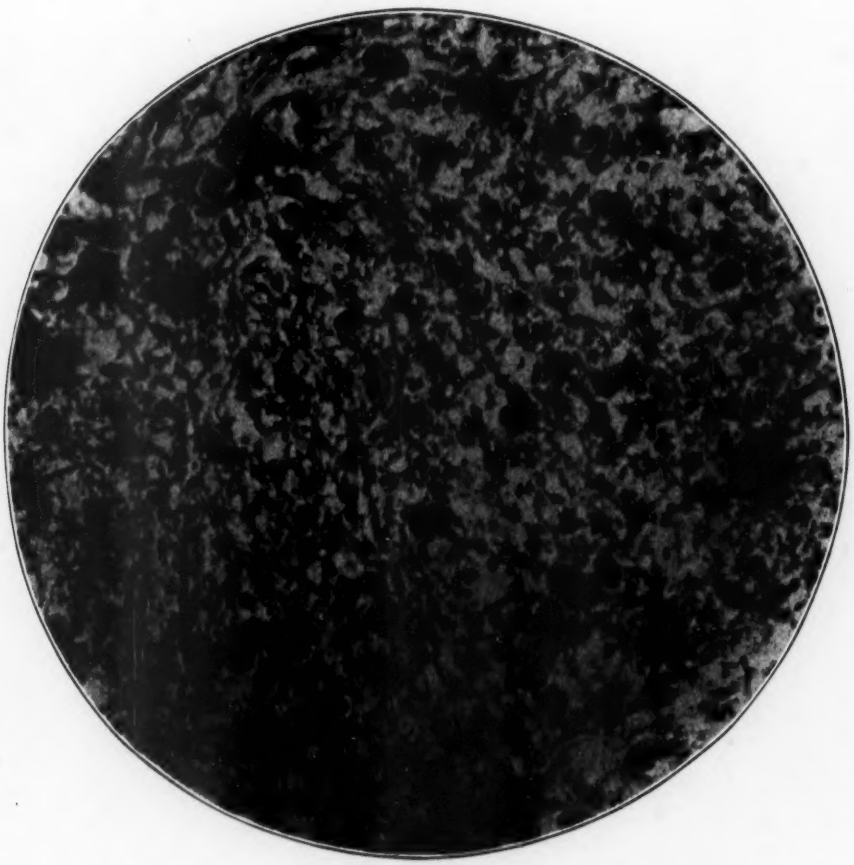

Fig. 29 (case 2).—Multinucleated groups of cells—oligodendrocytes.

decided on. The method of approach was satisfactory in this case as well as in case 3 and is apparently a safer route than that advocated by some others, since the nutrition of the globe was not seriously impaired.[3] The excellent postoperative appearance of the eye is note-

3. When this operation was performed I thought that it was an original procedure, since standard texts do not describe it. Subsequent review of the literature, however, revealed that H. Knapp performed a retrobulbar excision of the optic nerve for tumor as early as 1874. Many others have since employed retrobulbar removal of the tumors by various methods other than the well known Krönlein procedure.

worthy, as is the motility of the globe. At a recent examination the general appearance of the eye and the motility remained excellent, although five years have elapsed since the operation.

The postoperative picture of the fundus is of interest, since the retinal vessels contained blood. This no doubt was the result of anastomosis with the ciliary vessels. Pigmentary changes have been

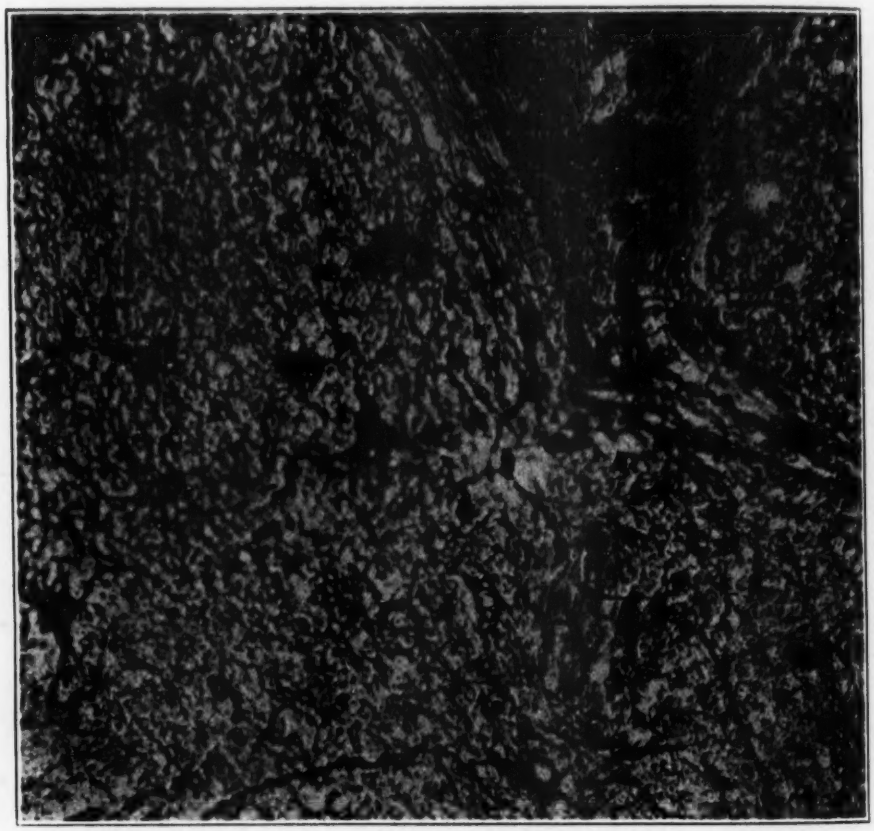

Fig. 30 (case 2).—Same section as in figure 26, showing neoplastic cells.

surprisingly absent. Evidently the ciliary vessels were not seriously injured at operation. This phenomenon has been noted by others, but usually after sectioning of the optic nerve the retinal vessels soon become mere threads and extensive chorioretinal pigmentary degeneration follows, as will be noted in case 3.

The deformity of the fibula and the scoliosis of the spine are of importance, the latter condition having been reported frequently in cases of Recklinghausen's disease (Brooks and Lehmann). The presence of

peripheral signs of Recklinghausen's disease of the abortive type, which was hereditary, is of outstanding significance (figs. 16 and 17).[4]

The tumor in this case was not so far advanced as that in case 1 and therefore afforded an opportunity for study of another stage of glioma of the optic nerve. In later stages of the growth the tumor advances so that it destroys most of the landmarks of the sheath as well as those of the nerve stem itself, so that conclusions regarding the precise

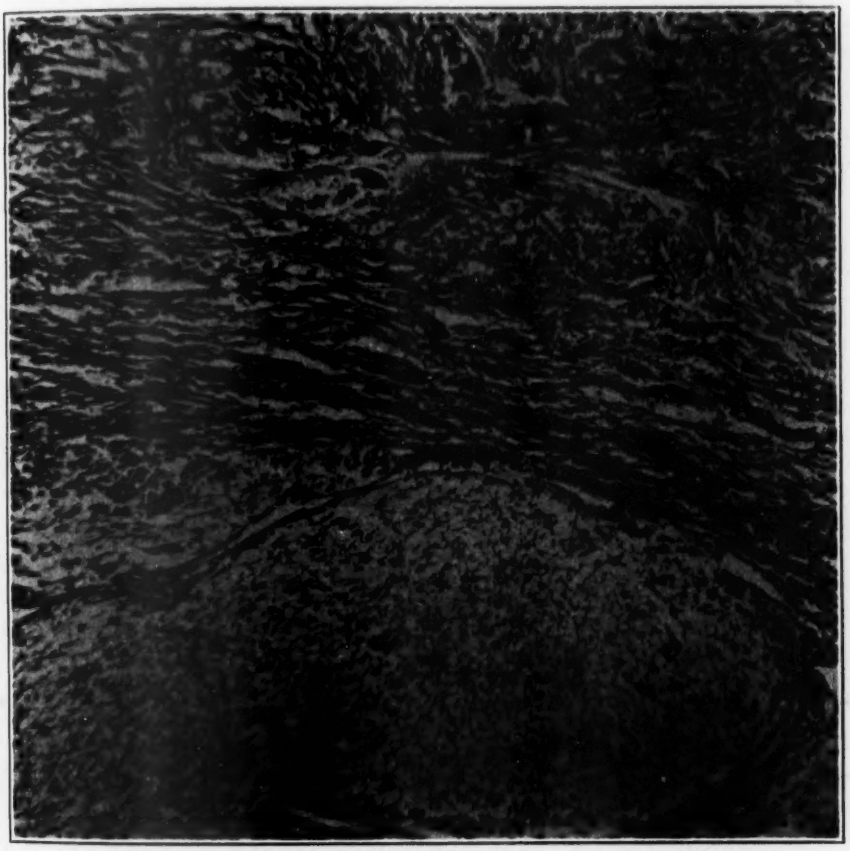

Fig. 31 (case 2).—Higher power magnification (× 150) of the section shown in figure 32. Note that the tumor in the nerve sheath is made up of coarse glial fibers, some straight and some wavy. Also note the almost total destruction of the pial sheath, which has been invaded and broken up by glial fibers. Few cytoid bodies are present. Phosphotungstic acid stain.

4. Slight enlargement of the right optic foramen was difficult to explain at the time the plates were made, since there was no clinical evidence of tumor formation in the right optic nerve. On readmission of the child since the completion of this paper there was definite evidence of an independent tumor developing in the right optic nerve.

nature of its development are rendered difficult—actually impossible in some recorded cases.

The study of this case indicates that the tumor arose within the nerve stem and spread outward to the sheath. This conclusion is more convincing when viewed in the light afforded by studies of the tumor in case 3.

Fig. 32 (case 2).—Transverse section through the nerve stem in the thickest area of the nerve (stage 3; phosphotungstic acid-hematoxylin stains; × 80). Note that the tumor in the nerve sheath is made up of masses of glial cells and fibers which have grown out from the nerve stem; also there is a thin layer of proliferated arachnoid cells beneath the dura (the dura is thin).

CASE 3 (fig. 34).—*Diagnosis of primary tumor of the optic nerve; retrobulbar excision of the anterior half of the optic nerve with preservation of the globe; gliomatosis of the optic nerve (operative specimen) with no involvement of the sheath or enlargement of the nerve; autopsy (four and one-half years later), showing glioma of the optic nerve invading the sheath, gliomatosis of the intracranial portion of the nerve, chiasm, pons and the medulla, a glioma in the temporal*

lobe of the brain, gliomatosis of the fellow nerve and Recklinghausen's phenomena, consisting of cutaneous café au lait–pigmented patches, plexiform neurofibromatosis of the ciliary nerves of the orbit, neurofibromatosis of the choroid, ciliary body and iris.

B. C., a girl aged 3 years, was first admitted to the ophthalmic ward of the Wisconsin General Hospital on Nov. 6, 1933. The child was born in the obstetric ward, there being no complications or unusual findings. She was

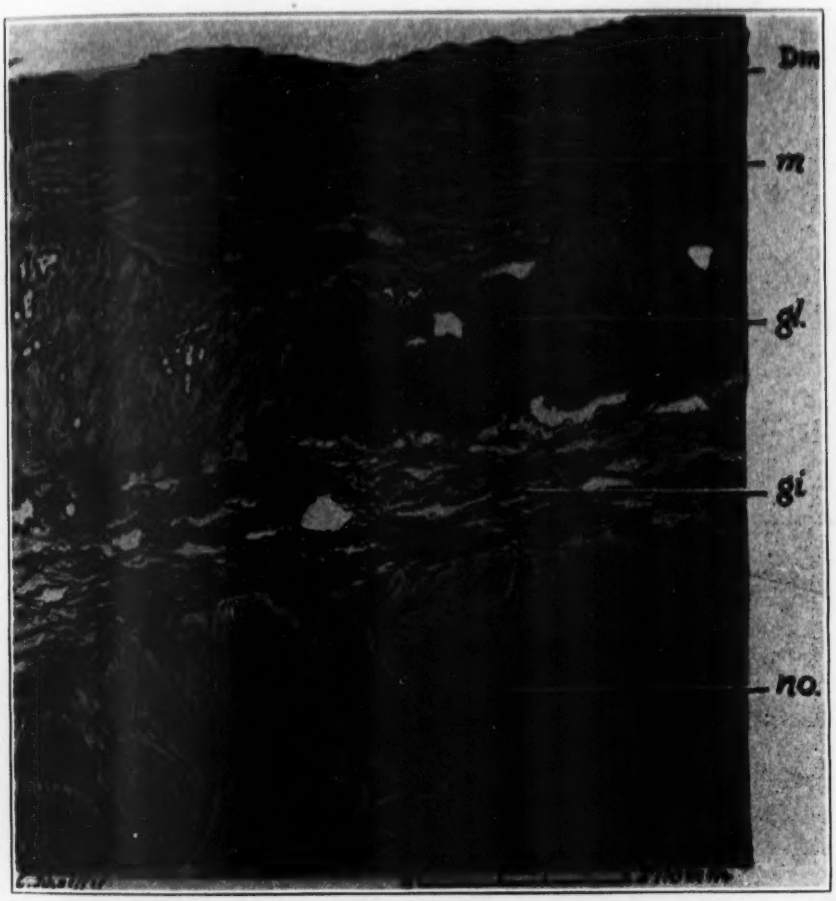

Fig. 33.—Diagrammatic drawing of a tumor of the optic nerve. (From Oberling and Nordmann: Les tumeurs du nerf optique, Ann. d'ocul. **164**:561-660, 1927.) *Dm* indicates the dura mater; *m*, meningioblasts; *gl*, glial proliferation; *gi*, pial sheath invaded by the glial tumor, and *no*, glioma within the optic nerve stem. These authors maintain the glial tumors of the sheath arise from the "meningioblasts" from the arachnoid sheath. Compare this figure with figure 32 (stage 3) and with figures 1 and 58, which suggest that the glial tumor of the sheath arises from the nerve stem and not from meningioblasts.

later brought to the pediatric outpatient department for observation because she was pale and had a burn on the leg which healed poorly. Exophthalmos of the right eye was noted at that time, and she was referred to the ophthalmic clinic.

Family History.—The child's mother had typical changes of mild Recklinghausen's disease. There were a number of pigmented patches on the skin and several soft mollusca fibrosa on the back and abdomen and one on the chin. Two of these soft tumors were excised, and microscopic study showed the usual patternless arrangement of the tissues which is found in neurofibromas of this type. The eyes of the mother showed a slight bilateral exophthalmos, which could not be attributed to disease of the thyroid. Examination of the fundi showed slight pallor of the nerve head in each eye. Vision was 20/30. The fields were within normal limits, though there was slight constriction.

General Examination.—Nothing of importance was found on general physical examination aside from a number of pigmented patches in the skin, one on the

Fig. 34 (case 3).—Gliomastosis of the optic nerve. Note the slight exophthalmos of the right eye (4 mm.) and also the slight convergence.

back of the neck measuring 3 by 3 inches (7.6 by 7.6 cm.), two large ones on the thigh measuring 1½ by 1½ inches (3.8 by 3.8 cm.) (fig. 35) and many smaller ones on other parts of the body. They were typical smooth, nonelevated, light coffee-colored spots, which the mother stated were present at birth. These spots were pale and had been completely overlooked or disregarded by three different examiners on three previous occasions.

There was exophthalmos of the right eye, measuring about 4 mm. (fig. 34). Slight ptosis was present, and there was definite limitation of motion in the field of the superior, inferior and external rectus muscles. There was slight convergence. The cornea was clear, and the anterior chamber was of normal depth. The pupil was larger than that of the left eye and was somewhat

irregular and eccentric, but it reacted to light and in accommodation. Examination of the fundus revealed clear media and a pale nerve head with sharp borders, the temporal half showing an unusually large physiologic cupping. Tactile tension was normal.

The left eye was normal.

The results of roentgen examination were reported as essentially normal, but a rereading of the plates later revealed an asymmetry of the bony orbits (fig. 36), the right being definitely larger than the left. The sella turcica itself appeared

Fig. 35 (case 3).—Café au lait-pigmented patches on the back and leg.

normal, but rereading of the films revealed a small, narrow pear-shaped shadow under the anterior clinoid process.

A tentative diagnosis of tumor of the optic nerve was made, and it was requested that the child be brought in for periodic observation. A second examination three months later (Jan. 10, 1934) revealed what appeared to be a slight increase of the exophthalmos of the right eye, though the exophthalmometer reading was unsatisfactory due to lack of cooperation. The convergence was definitely increased, measuring 5 to 10 degrees, with some limitation of motion but no paralysis of the extraocular muscles. The pupil reacted normally but was somewhat irregular and still eccentric, being drawn toward the temporal side.

The iris showed definite atrophy. It was somewhat thinned and had an ironed-out appearance. It dilated to 7 mm. with homatropine hydrobromide. The media were clear. The disk was seen with a —2.00 sphere, and the temporal pallor had increased and was to be seen in the nasal half of the disk as well as in the temporal portion. The cupping was considered physiologic, though it was unusually large and deep, and so was regarded with suspicion. The vascular system was normal. The vision was estimated with difficulty, owing to the age of the patient, but that of the right eye appeared to be definitely reduced.

Roentgen examination showed the same asymmetry in the size of the orbits as previously noted as well as the anterior necklike shadow under the anterior

Fig. 36 (case 3).—Roentgenogram of the skull. Notice the enlargement of the right bony orbit, which was due to plexiform neurofibromatosis of the nerves of the orbit.

clinoid process (fig. 37). Stereoscopic plates revealed no abnormality of the body of the sella turcica.

The left eye was normal, though the disk appeared slightly pale.

A diagnosis of tumor of the right optic nerve was made, and operation was advised.

Operation (Jan. 31, 1934).—Anesthesia was produced by the endotracheal administration of nitrogen monoxide and ether. Exploration of the right orbit was done as outlined in case 2, through an incision in the skin along the lower bony rim, the orbit being entered directly through the septum orbitale (fig. 38). The nerve was exposed with greater difficulty than in case 2. At the time of operation this

Fig. 37 (case 3).—Sella turcica (actual size). Note the pear-shaped shadow which projects forward from the upper anterior aspect of the body of the sella under the anterior clinoid process.

Fig. 38 (case 3).—Appearance of the patient one month after operation (retrobulbar excision of one half of the optic nerve). Note the line of incision in the lower lid; this disappeared after complete healing (see figure 43).

was attributed to the smaller size of the bony orbit in a child of 3 years of age. The nerve was tied off with catgut where it joined the globe and also near the middle of the orbit, and a section about 11 mm. in length was excised. The wound was closed as described in the previous case, and the lids were sutured together with a mattress suture, since I anticipated some trophic change in the cornea.

There was moderate postoperative reaction and swelling, though not nearly so marked as in case 2, and healing progressed so that the dressing was removed in three weeks. The suture was removed from the lids on the tenth day after operation. The cornea was found to be clear and the pupil fairly well dilated from atropine, which had been used daily. The action of the lids was good, and the extraocular movements, which had been absent, began to return feebly. The child was discharged four weeks after operation and was observed from time to time in the outpatient department.

Microscopic Examination (section of the optic nerve removed at operation).—Grossly the nerve appeared of about normal size throughout the portion excised, measuring about 3 mm. in diameter (fig. 39). Sections revealed no thickening

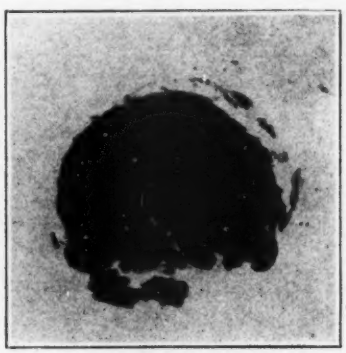

Fig. 39 (case 3).—Transverse section through the optic nerve (× 11). Note that the sheath is not involved. The dural sheath was injured on removal of the nerve.

of the dura or arachnoid, nor was there any infiltration in the intervaginal spaces in any part of the nerve. The pia was intact, but both the arachnoid and the dura were considerably thinner than in the normal preparations, probably due to trauma in isolating the nerve from surrounding structures. Transverse sections of the nerve (fig. 40) appeared strikingly normal to casual inspection. The general architecture of the nerve was preserved, though there was some enlargement of the funiculi. Careful study revealed a vacuolation of the tissue within the funiculi and condensation of glial fibers which bordered the fibrous septums (fig. 41). Staining with phosphotungstic acid and hematoxylin showed a marked increase in glial fibers, especially adjacent to the septums. The glial cells throughout the funiculi were increased both in size and in number. Vacuoles which appeared throughout the funiculi were found to be due in part to vacuolation of the glial cells and in part to actual holes. The latter appeared to be attributable to shrinkage or to complete atrophy and disappearance of the nerve fibers. A few of the myelin sheaths were present in some areas, but they had completely disappeared throughout most of the sections examined. The vacuolation of the tissue

within the funiculi was similar to that observed in the sections in cases 1 and 2, though not so extensive, while formation of glial fibers was not so advanced.

Subsequent Clinical Data (July 23, 1934).—Six months after operation, according to notes made at the time, there was still slight exophthalmos with some widening of the palpebral fissure. The incision in the skin showed a faint linear scar. There was some fulness above and below the orbital rim. Ocular motility was free in all fields, with a tendency to convergence at times—about 5 degrees, as seen before operation. The globe was somewhat larger than that on the left side. The cornea remained clear; it appeared slightly larger than that of the left eye. The anterior chamber was of fair depth; the aqueous was clear; the

Fig. 40 (case 3).—Transverse section of the nerve (hematoxylin and eosin; ×200). Note the normal architecture of the bundles of nerve fibers, the marked increase in glial cells and beginning condensation of fibers bordering septums.

pupil was very irregular and displaced temporally upward, measuring about 5 mm. in its longest axis, and the iris appeared atrophic. There appeared to be a slight consensual reaction to light; the media were clear; the fundus showed extensive degeneration of retinal pigment, and large masses appeared throughout the retina, one mass lying directly over the disk and obscuring its outline, though its pallor could be seen. The vessels were narrow and apparently bloodless.

A note made one year later (July 5, 1935) stated that there was little change in the eye since the previous examination. There appeared to be slight swelling of the lids of the right eye. Exophthalmos was slight and unchanged from that last recorded. The cornea was clear; the extraocular movements were

normal, and the anterior chamber was a little shallower than normal. The pupil was very irregular and displaced temporally and upward; it measured 5 mm. at its longest axis and was pear shaped (figs. 42 and 43). The iris was atrophic; the fundus appeared as previously described.

Examination on March 16, 1936, showed little if any change from that of July 23, 1934. Lateral stereoscopic roentgenograms of the sella turcica were again made and revealed a necklike, pear-shaped shadow extending from the

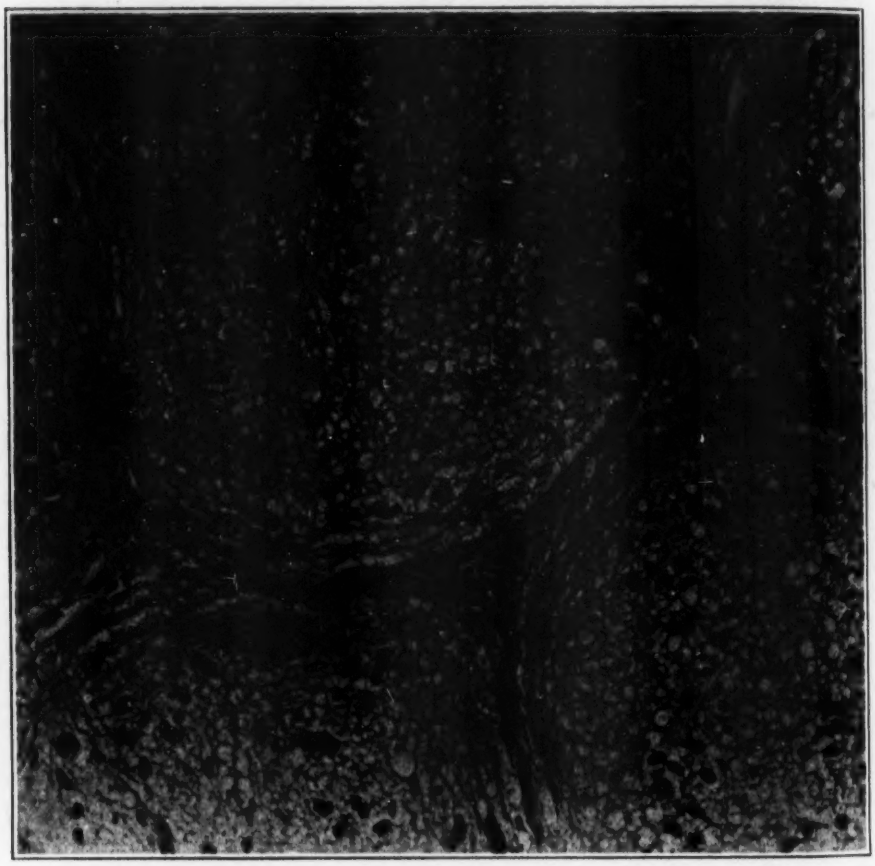

Fig. 41.—High power magnification of the section in figure 40. Note the vacuolation of glial cells and the holes in the glial framework of the nerve. The nerve fibers had largely atrophied.

upper edge of the body of the sella turcica under the anterior clinoid process. The optic canals were reported about equal in size and shape and within normal limits in diameter. The cranial bones were thin.

On Sept. 16, 1936, two and one-half years after operation, examination revealed slight exophthalmos and fulness of the lids of the right eye. There was a faint scar in the lower lid at the line of suture. The cornea was clear; the anterior chamber was deep; the pupil was larger than the left and still eccentric; the media were clear; the fundus showed extensive pigmentary degeneration of the

choroid and retina, and no retinal vessels were visible. The optic nerve showed advanced atrophy and was partially covered by a mass of pigment. The left eye appeared normal aside from a definite pallor of the nerve head, which had increased

Fig. 42 (case 3).—Photograph was taken four and one-half years after operation at the age of 7. The right cornea is slightly larger than the left. Note the pear-shaped coloboma of the pupil due to contraction from neurofibromatosis of the iris. There is paresis of the left facial nerve. Note the excellent position of the globe and the faint line of scar.

Fig. 43.—Closer view of the patient's eyes, showing distortion of the pupil of the right eye resembling a pear-shaped coloboma. Note the faint line of scar in the skin of the right lower lid—the site of orbital exploration.

since the previous examination. Vision in the left eye was 20/30 — 2 with a + 1.00 sph. ⊃ + 1.50 cyl., axis 90. The school nurse reported that the child was having difficulty with close work in school.

The child was readmitted to the hospital for study six months later (Feb. 25, 1937). At that time slight exophthalmos of the right eye was noted (2 mm. greater than the fellow eye), with definite fulness of the upper and lower lids. The line of incision made at operation was barely visible. Nothing could be palpated in the orbit. The eyes were straight, and ocular movements were free in all fields. The cornea of the right eye remained clear, and the anterior chamber was of fair depth. The pupil was more drawn to the temporal side and measured 4 by 5 mm. A consensual reaction to light seemed to be present, though slight. The pupil dilated well with hematropine hydrobromide. The iris appeared atrophied. Examination of the fundus revealed a few coarse floating bodies in the vitreous. The lens was clear. The fundus picture had changed little. The color reflex was pale, but the entire retina was covered with patches of pigment. Some white patches were seen which appeared like masses of glial tissue or scar tissue. The retinal vessels were absent, only a few faint, thin remnants in the form of fibrotic threads being visible. The disk was indistinctly seen and appeared white. It was obscured by masses of retinal pigment.

Fig. 44 (case 3).—Roentgenograms of the optic foramens (actual size). Both foramens are slightly enlarged, that of the right side being definitely the larger. (The photographs were taken one and one-half years after the first observation.)

The left eye appeared normal aside from definite atrophy of the optic nerve. The disk was oval and flat, and the atrophy was considered grade 2. The vessels appeared normal. The vision was 20/30 —2.

Roentgen examination showed that the asymmetry in the size of the orbits, which was present in the original films, had remained unchanged. Roentgen studies of the optic foramens showed definite changes, the right foramen being larger than the left. Measurements made on the films (fig. 44) showed the right optic foramen to have a transverse diameter of 7.5 mm. and a vertical diameter of 6.8 mm.; the transverse diameter of the left optic foramen was 6.8 mm. and the vertical diameter 5.6 mm.

There was some stippling of the bones of the vault.

The pigmented patches in the skin showed no change. The child appeared to be in good health.

Brief observation in the clinic three months later (Jan. 3, 1938) showed the visual acuity in the left eye to be 20/100. Owing to my absence at this

time, no special studies were made. The child was next seen on March 10, 1938, which was about one year after I had last seen her. She was admitted to the wards for further study. The patient, now aged 7, had developed physically as a normal child, though her mentality was definitely below that of children of her age. Her mother reported that she had vomited at intervals for several weeks. The vomiting had been sudden and projectile in type. She had not been ill otherwise and did not complain of headaches. Neurologic examination revealed paresis of the left facial nerve, central in type, with exaggerated knee jerks and a suggestive Babinski sign.

Examination of the right eye showed slight exophthalmos, which measured 3 mm. greater than that of the left eye. There was also slight ptosis. The extraocular movements were normal. The cornea was clear except for a faint opacity in the outer layers of the stroma extending across the lower third. The anterior chamber was slightly deeper than in the left eye. The pupil was pear shaped and drawn to the temporal side (fig. 43); it was inactive to light. The iris was abnormal, showing definite atrophy. Its markings were obliterated and its color faded and blotchy. The lens was clear. There were a few floating shred-like opacities in the vitreous. The fundus showed extensive chorioretinal pigmentary degeneration, as previously described. Tension appeared normal in each eye to touch. Vision in the right eye was nil.

The left eye appeared normal aside from fairly advanced atrophy of the nerve head. The outlines of the disk were sharp and distinct. Vision was 20/100. The field appeared somewhat contracted, though accurate measurement was difficult due to poor cooperation.

Roentgenograms of the skull revealed definite changes when compared with films made the previous year. Lateral views showed a marked increase in the size of the necklike shadow which extended anteriorly from the upper rim of the body of the sella turcica under the anterior clinoid process (fig. 45). When the skull was viewed in perfect lateral position, there was a large, bulbous, slightly pear-shaped shadow; when the head was slightly tilted, a double shadow was seen (fig. 45). The shape of the body of the sella turcica was unchanged from that revealed at the previous examination, though it and the skull as a whole were larger, due to natural growth. The skull showed digital markings throughout the vault, suggestive of intracranial pressure (fig. 45). The right orbit remained unchanged. The right optic foramen had increased slightly in size.

A diagnosis of intracranial tumor was made. It was considered likely that the tumor in the unremoved portion of the optic nerve had extended back into the chiasm. The patient was therefore referred to the department of surgery. Further studies by Dr. E. R. Schmidt, which included a ventricular puncture (April 7, 1938), confirmed this diagnosis. A ventriculogram (read by Dr. W. J. Bleckwenn) revealed the left ventricle to be larger than the right. No third ventricle was visualized. In the lateral view the right ventricle showed a defect, the temporal horn being cut off near the ampulla. The lateral body of the ventricle was pushed upward, giving the impression of a lobulated tumor in the right temporal lobe. There was a slight shift of the right ventricle to the left. The reading suggested a subcortical tumor.

Operation (April 30, 1938).—Dr. E. R. Schmidt performed a right fronto-parietal craniotomy. The right optic nerve was exposed and found to be considerably enlarged. A tumor was encountered in the anterior and medial portion of the right temporal lobe. The chiasm appeared slightly enlarged, but no definite tumor was found. The tumor being inoperable, the right optic nerve extending into the chiasm was removed, as was a small section of the tumor. After this

considerable bleeding developed, which was promptly controlled by electrocoagulation. The patient was given a transfusion on the operating table. The bone flap was replaced and the wound closed. The patient was returned to the ward and died ten hours later.

General Autopsy (Dr. J. L. Parks).—A complete postmortem examination was made, and the right eye and orbital contents were removed. The general observations included postmortem ulceration and perforation of the stomach and left side of the diaphragm, digestive necrosis of the peritoneum, omentum and left pleura and pancreatic necrosis. The pituitary body showed hemorrhage and necrosis in the anterior lobe.

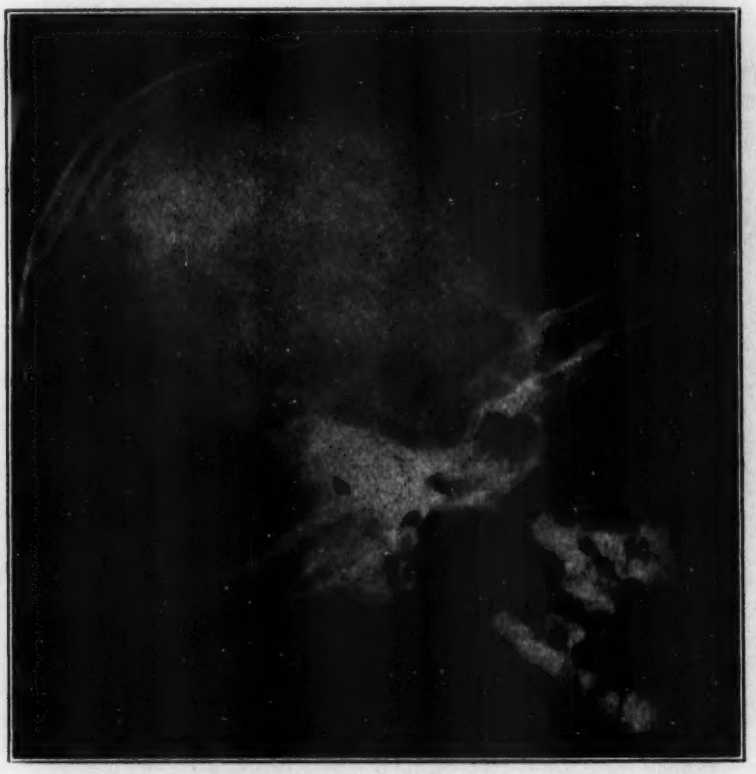

Fig. 45 (case 3).—Roentgenogram of the skull taken four years after the first observation. Note the increased depth of the sella turcica and marked increase in the size of the pear-shaped shadow. There are digital impressions in the vault, due to increased intracranial pressure.

Macroscopic Study of the Brain (Dr. J. C. McCarter).—According to the report made, there was a gliomatus tumor measuring about 4 by 4 by 3 cm. in the anterior and medial portion of the right temporal lobe. The tumor was firm and gray and showed some irregular cystic softening. It had fairly clear borders but was not encapsulated (fig. 46).

The tumor had destroyed and presented to the surface in the region occupied by the hippocampal gyrus. It compressed the inferior convolutions of the temporal

lobe and compressed and pushed laterally the inferior horn of the right lateral ventricle. It partially destroyed the inferior portion of the right lenticular nucleus and approached but did not invade the posterior limb of the right internal capsule.

The hypothalamic region was covered with clotted blood, and the relations of the optic nerves and chiasm could not be clearly made out. The chiasm did not appear to be especially enlarged.

The posterior portion of the tumor caused pressure across the fissure between the temporal lobe and cerebral peduncles, and the optic tract on the right could

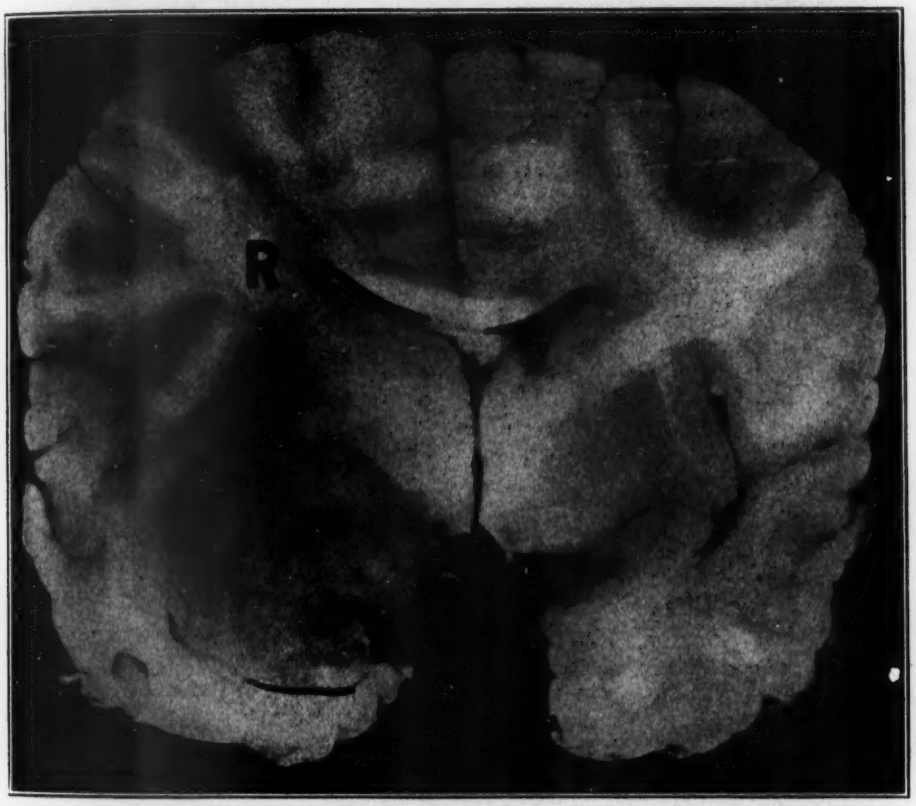

Fig. 46 (case 3).—Section of the brain. Note the tumor (glioma) in the left temporal lobe.

not be identified owing to atrophy from this pressure. The optic tract on the left was identified, but appeared atrophic with minute cystic changes.

The corpus striatum, the thalamus, the pons and the medulla oblongata were definitely enlarged and extremely firm. These regions were pale, and the normal contrast between gray and white matter was much reduced.

There was evidence of recent trauma (evidently due to operation) about the tip of the right temporal lobe, about the optic chiasm and at the base of both frontal lobes in the olfactory trigons.

Microscopic Study of Brain Tissue (Dr. J. C. McCarter).—A cross section area of the medulla (fig. 47) was about twice the normal size for an adult. The nerve cells were few in number and sparse in distribution, and many remaining ones showed cloudy swelling and chromatolysis. No demyelination was demonstrated. There was a striking increase in the number of astrocytes with the formation of many fibrils, which were isomorphic in distribution.

The changes in the pons were similar to those in the medulla. Several giant astrocytes were seen.

The cerebellum showed some increase in astrocytes in the white matter.

The changes in the thalamus were similar to but not as great in degree as those in the medulla.

The chiasm showed changes similar to those noted in the medulla, though the chiasm was but slightly enlarged. Small atrophic areas replaced by vacuolated tissue were seen. The nerve cells in the adjoining hypothalamus showed swelling and chromatolysis.

The tumor was an astrocytoma, showing evidences of increasing malignancy and less differentiation (fig. 48).

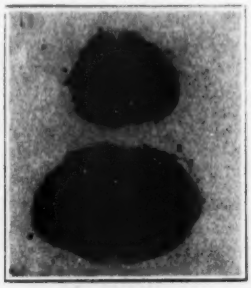

Fig. 47 (case 3).—Upper section, medulla from a normal adult, actual size. Lower section, enlarged medulla with diffuse gliosis; also actual size.

The tumor showed marked cystic degeneration in which large spaces were filled with a clear, structureless material. Much of the tumor was so necrotic that it stained poorly by any method. The cells appeared of mixed types, some having the appearance of unipolar and bipolar spongioblasts and others resembling swollen protoplasmic astrocytes.

Study of the Eye and Orbit, Region of the Hypothalamus, Chiasm and Optic Nerve.—The eye, together with the surrounding soft parts of the orbit, was removed at autopsy and placed in a 10 per cent dilution of formaldehyde. The specimen was cut transversely in three parts after the globe was severed. One section was mordanted for Weigert staining, one was refixed in Zenker's solution and the third was left in formaldehyde.

No satisfactory macroscopic study could be made, since I did not wish to disturb the relation of the tissues about the nerve. The cut end of the nerve at the apex of the orbit appeared definitely enlarged to about twice its normal size, with some thickening of the sheath. One part of the nerve (approximately one-third on cross section) on gross inspection appeared darker in color than the other two-thirds. The chiasm and region of the hypothalamus were slightly

enlarged but showed no definite tumor formation on gross inspection. The right optic nerve and a small section of the chiasm were missing from the postmortem specimen, since they were removed at operation. A short section of the left optic nerve was seen as it entered the chiasm. The intracranial portion of the nerve removed at operation was fixed in formaldehyde–ammonium bromide as well as in Zenker's solution. It appeared to be about twice the normal size but showed no gross evidence of tumor about the sheath.

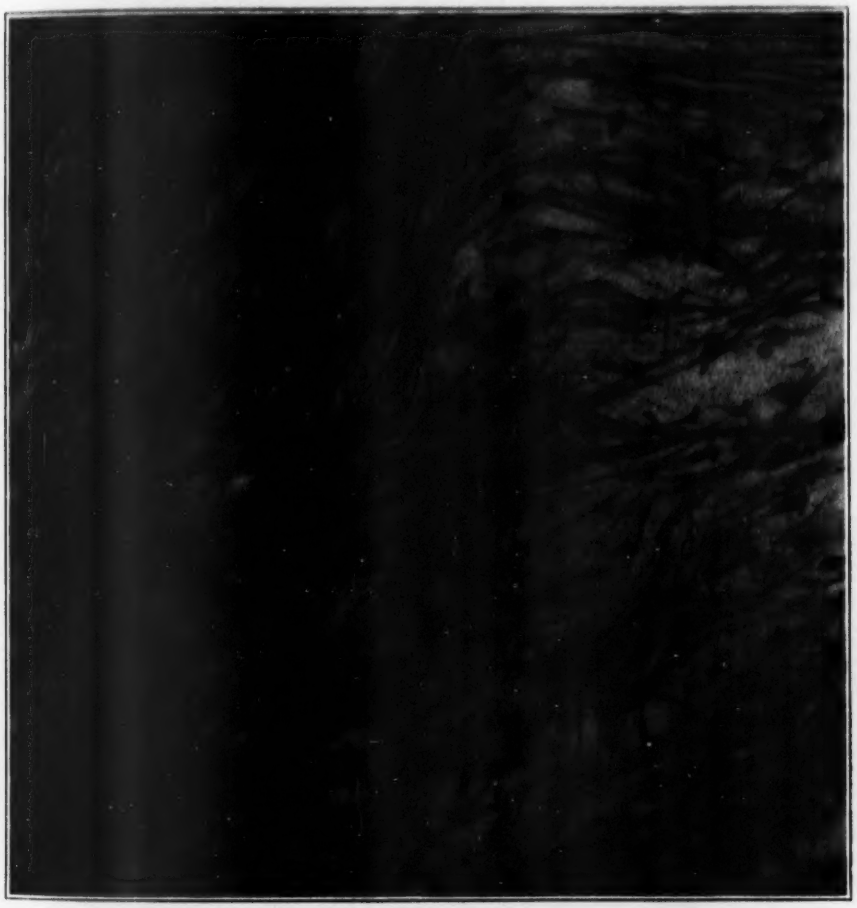

Fig. 48 (case 3).—Section from the tumor of the brain.

Microscopic Study of the Optic Nerve: Part of the operative specimen of the nerve was sectioned after freezing; the remainder was embedded in paraffin. The postmortem specimen, including the eye and orbital contents as well as the chiasm, was serially sectioned. Various methods of staining were used, including hematoxylin and eosin, Van Gieson's stain, Mallory's phosphotungstic acid–hematoxylin stain, Mallory's trichrome stain, Weil's iron hematoxylin, Weigert's myelin sheath stain, the Pal-Weigert stain, Cajal's gold chloride stain, the Del Rio Hortega and Weil-Davenport ammoniacal silver methods for astrocytes and oligodendrocytes, and others.

The intracranial section of the optic nerve, removed at intracranial exploration, included a small part of the chiasm where the nerve entered it. The nerve was oval and about twice its normal size. It showed marked proliferation of the glial cells, with some fiber formation. These fibers were grouped about the connective tissue septums and the pia. The pia was intact and showed only slight invasion by glial fibers in a restricted area. The arachnoid, where present, showed no abnormal proliferation or thickening, such as was noted in the intraorbital part of the nerve. The histologic picture bore a striking resemblance to the sections of the nerve removed at the first operation.

The sections of the chiasm, optic tracts and the stub of the left nerve were serially sectioned, but for some reason staining was not satisfactory. Marked glial proliferation of the right nerve, which adjoined the chiasm, was found, the sections staining well with various methods, with the exception of the silver methods. Here, though the specimens were cut from frozen sections, the technic was not entirely satisfactory. There appeared to be moderate glial hyperplasia throughout this region but no evidence of tumor formation.

The intraorbital part of the nerve (autopsy specimen) showed considerable variation, depending on the level at which the nerve was sectioned. Serial sections revealed that the main body of the tumor occupied a position a little posterior to the point where the nerve had been cut at the original operation four years previously. The nerve stem was slightly oval and measured 4 by 7 mm. (slide section). Surrounding this, the sheath was thickened and increased the diameter over all to 6 by 9 mm. The size gradually diminished toward the apex of the orbit, where the nerve stem itself was about half again the size of the normal nerve, with a corresponding thinning of the part of the tumor which invaded the sheath.

Anterior to the cut end of the nerve was a tangled mass of connective tissue, which filled the space formerly occupied by the nerve. This extended up to the globe. It contained numerous ciliary nerves, for the most part cut transversely. These were much enlarged and showed varying stages of proliferation of tumor cells. The appearance was fairly typical of that generally described as plexiform neurofibromatosis (fig. 49). As the sections approached the globe, the tissue was made up largely of a tangled mass of connective tissue and strands of collagen. There was no remnant of the original optic nerve, since it had been excised.

Where the sections approached the cerebral end of the nerve, which was not excised at the original operation, traces of the sheath first appeared. The dural sheath was first identified, and sections gradually disclosed its normal contour. It appeared fairly normal, though thickened. Lying within the lumen of this dural envelop there was a mass of proliferated arachnoid cells. As the sections extended farther back toward the apex of the orbit, traces of the nerve stem began to appear. This consisted of dense masses of glial fibers; it stained deep blue and was embedded in a meshwork of pink-staining tissue (phosphotungstic acid and hematoxylin), which apparently arose from the pial lamellae. These bands of fibers criss-crossed in no definite pattern and had the appearance of collagen, no definite nuclei or cells appearing in them. Surrounding this there was a thick layer of proliferated arachnoid cells which was sharply limited in a bandlike sheath. Isolated cells were typical flattened ones with short, oval nuclei, though some showed marked enlargement of the nuclei. This area of proliferated arachnoid cells stained light pink in sharp contrast to the dense blue of the glial elements within the nerve stem and pia, and no glial fibers penetrated it. As the sections were followed back, the architecture of the nerve and its enveloping sheath

assumed a more orderly arrangement, but the nerve stem and surrounding tumor gradually increased in size (figs. 50, 51 and 52).

Microscopic study of sections from the thickest area of the tumor revealed the following picture: The nerve stem showed the usual arrangement of the funiculi separated by connective tissue septums (fig. 53). The funiculi, however, were markedly enlarged and their shape distorted. The septums were present, while the intraseptal spaces were compressed in places and distended in others. The most striking feature of the section was the enormous overgrowth of glial cells and fibers. The fibers occupied and filled the entire area of the funiculi. They were most

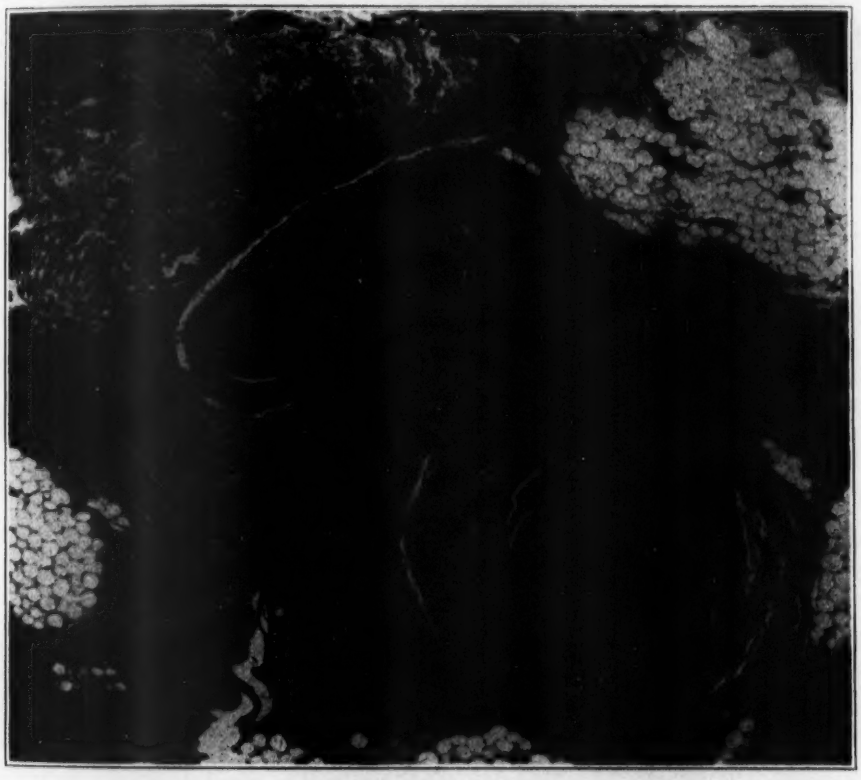

Fig. 49 (case 3).—Plexiform degeneration of the nerves of the orbit. Note the three large degenerated nerves.

dense about the borders of the funiculi, where they abutted the connective tissue septums (fig. 54), but they were not so sharply limited to this area as those in the original section of the nerve or those in the sections described in cases 1 and 2. The glial fibers invaded the intraseptal spaces in many places, though they did not destroy them. No trace of nerve fibers could be found by either Weigert's or Weil's stain.

The nuclei of the cells showed the same variations as those described in the original operative specimen and in sections from the specimens in cases 1 and 2. These were large oval and round forms, with some of irregular contour, especially

imperfectly oval (figs. 55 and 56). Many of these oval nuclei were more slender or elongated, especially where the glial fibers were most dense. The predominant nuclear forms were similar in outline to those of astrocytes, as depicted by Penfield in his diagrammatic drawings in his "Cytology and Cellular Pathology of the Nervous System." The nuclei were best studied with ordinary hematoxylin and eosin stains. Many were hyperchromatic, and multinucleated groups were frequently seen, probably the result of cell division (fig. 56). With Mallory's phosphotungstic acid and hematoxylin stain, the fibers were so intensively and selectively stained that outlines of the nuclei were somewhat obscured (fig. 57).

Fig. 50 (case 3).—Transverse section through the nerve and surrounding tumor (removed four and one-half years after the specimen in figure 39). Note the ciliary ganglion at the top of the illustration and the glioma of the optic nerve at the bottom.

The fibers varied in different parts of the nerve. They were coarse and somewhat angulated in some areas, while in others they were more wavy. Some of the fibers appeared to be thick cytoplasmic projections, some running straight for long distances and others being angulated. Small dots, densely stained, appeared in these processes, especially at the terminal ends. These dots in some ways resembled the gliosomes described as normally present in the processes of protoplasmic astrocytes.

The more typical glial fibers penetrated the pial sheath in innumerable places throughout most of the circumference of the nerve (figs. 1 and 58). The pial sheath was somewhat thickened, though separated into layers, between which dense masses of glial fibers had grown. These fibers in places left the nerve in dense sheaves, similar masses often distending the pial lamellae. They penetrated the pia frequently along the borders of the funiculus where the septal prolongations from the pia entered the nerve. They often left the nerve, however, directly through the pia bordering the central area of a funiculus. The sheaves of glial fibers in the pia often appeared without cellular or nuclear attachments, though this may have

Fig. 51 (case 3).—Section of the nerve farther back, toward the apex of the orbit.

been the result of an inability to follow a fiber throughout its course. These glial fibers appeared to run concentrically around the nerve, the dense blue-stained masses alternating with the reddish pink strands of the pia (phosphotungstic acid–hematoxylin stain). They extended just beyond the pia, stopping short of the thickened arachnoid layer beyond, though in one limited area they invaded it a short distance.

The arachnoid sheath was replaced by an enormously thickened mass of tissue made up of proliferating arachnoid cells and some strands of collagen (figs. 1 and 59). These cells resembled, and in places were identical with, the mesothelial cells which

normally line the subdural space and cover the outer aspect of the arachnoid sheath. In one area they assumed an arrangement slightly suggestive of a whorl which surrounds a psammoma body (fig. 60). Other isolated, homogeneously blue-stained bodies had the appearance of typical corpora arenacea (fig 61). Most of the cellular proliferation in the arachnoid, however, appeared in sheets or masses of cells, similar to the meningiotheliomatous type of meningeal tumors described by Bailey and Bucy. They were not divided into lobulated masses, nor did they otherwise resemble the typical dural endotheliomas or meningiomas which are found

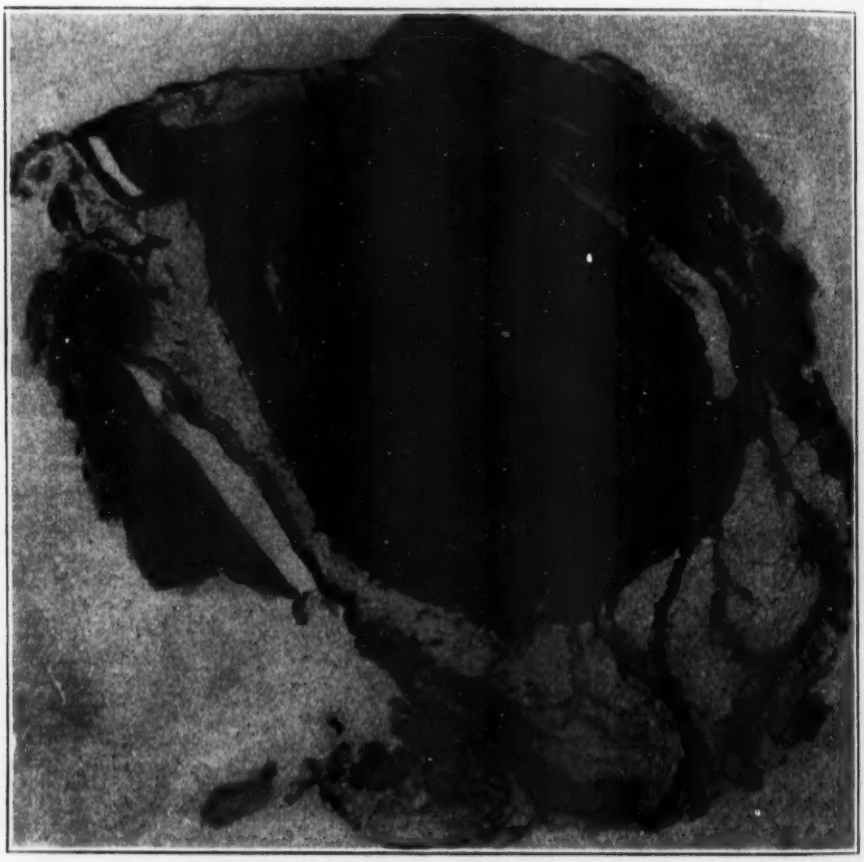

Fig. 52 (case 3).—Section through the thickest area of the tumor. Note the marked enlargement of the nerve stem, the proliferation of the arachnoid cells surrounding the nerve stem and the thickened ciliary nerves outside the sclera.

both in the optic nerve sheath and in the brain. Differential stains, particularly Mallory's phosphotungstic acid-hematoxylin stain, brought out in marked contrast the sharp limitation between the glial elements on the one side and the mesoblastic or mesothelial elements on the other, which made up the growth in the arachnoid sheath. The latter mass took a light pink stain with light blue nuclei, while the glial elements took a deep purplish stain. The sharp differentiation of the glial

elements also was clearly shown by other stains, such as Mallory's trichrome stain, aniline blue, Weil's iron hematoxylin, and Van Gieson's stain. The last-mentioned stain was less satisfactory due to the peculiar yellowish brown color it imparts to the normal arachnoid cells. A few cytoid bodies were found in the dense masses of glial fibers within and without the nerve stem. Outside the growth in the arachnoid sheath, the dura, much thickened, surrounded the tumor.

Small blood vessels were seen in the neural portion of the tumor only within the intraseptal spaces. A few small vessels were also present in the area of pro-

Fig. 53 (case 3).—Transverse section through the posterior half of the nerve (removed four and one-half years after the original operation); hematoxylin and eosin; × 200. Note the enormous increase in glial cells and fibers. (Compare with figure 40, which shows the same nerve when the tumor was in its earliest stage.)

liferated arachnoid. A striking feature of this tumor was the complete absence of vacuolated spaces within the nerve stem. The neuroglial fibers were so numerous and their growth so dense that every vestige of the vacuolated pattern observed in the nerve removed at the original operation had vanished (fig. 57). There were no vacuolated spaces in the thickened tumor in the arachnoid sheath, but the absence

of neuroglial tissue here no doubt accounted for this. As the sections approached the apex of the orbit, the nerve became much smaller and the sheath became thinner. The glial proliferation was unevenly distributed in the nerve stem, one sector showing a massive cellular proliferation, while the remainder of the nerve showed a much milder involvement. This could be seen macroscopically where the nerve was cut at the optic foramen, as previously noted. This uneven distribution of the glial cells extended back into the intracranial portion of the nerve, but was here much less distinct.

Fig. 54.—Same section as shown in figures 53 and 55 (phosphotungstic acid stain; × 200). Note the marked condensation of glial fibers which border connective tissue septums. The interseptal spaces are dilated, and some contain glial fibers (upper right side).

There were other variations in the sections as one approached the chiasm. The vacuolated spaces again appeared, and fiber formation was less pronounced.

Examination of the Globe and Orbital Contents Outside the Nerve: A complete description of the globe and orbital contents has already been published.[5]

5. Davis, F. A.: Plexiform Neurofibromatosis (Recklinghausen's Disease) of Orbit and Globe: With Associated Glioma of the Optic Nerve and Brain; Report of a Case, Arch. Ophth. **22**:761 (Nov.) 1939.

Briefly, the study revealed extensive neurofibromatosis of most of the nerves, including the ciliary ganglion. Numerous microscopic tumors were found along the course of the nerves (figs. 62 and 63). They showed varying stages of degeneration, from slight thickening to complete disorganization (fig. 64). Some had progressed to a point of partial liquefaction, such as Antoni described in the reticular type of neurinoma, type B (figs. 64 and 65).

The eye was slightly larger than normal. It showed marked thickening of the uveal tract due to extensive neurofibromatosis of the myelinated and nonmyelinated

Fig. 55 (case 3).—Same section shown in figure 53 (hematoxylin and eosin; ×350). Note the multinucleated groups of cells. Glial fibers have obliterated the holes noted in figure 41.

nerve fibers (fig. 66). The choroid was about four times its normal thickness in places. The filtration angle was completely obliterated from the adhesion of the thickened iris to the posterior surface of the cornea.

The ciliary nerves throughout the sclera, especially in the posterior segment, were much enlarged due to marked overgrowth of all the supportive elements of the nerves, with degeneration of the myelin sheaths of some of the nerves.

This eye was unquestionably in an early stage of buphthalmos, brought on by blockage of the filtration angle from adhesion of the newly formed tissue of the iris to the posterior surface of the cornea.

Advanced buphthalmos associated with plexiform neurofibromatosis of the lids, orbit and uveal tract is a well recognized, though rare, condition. It is one of the varied manifestations of Recklinghausen's disease.

Diagnosis.—A diagnosis was made of Recklinghausen's disease, manifested by abortive peripheral lesions—café au lait spots; plexiform neurofibromatosis of the orbit; neurofibromatosis of the choroid, ciliary body and iris; glioma of the optic nerve (type, astrocytoma); gliomatosis of the left optic nerve, chiasm, medulla, pons and thalamus; glioma of the temporal lobe of the brain, and early buphthalmos.

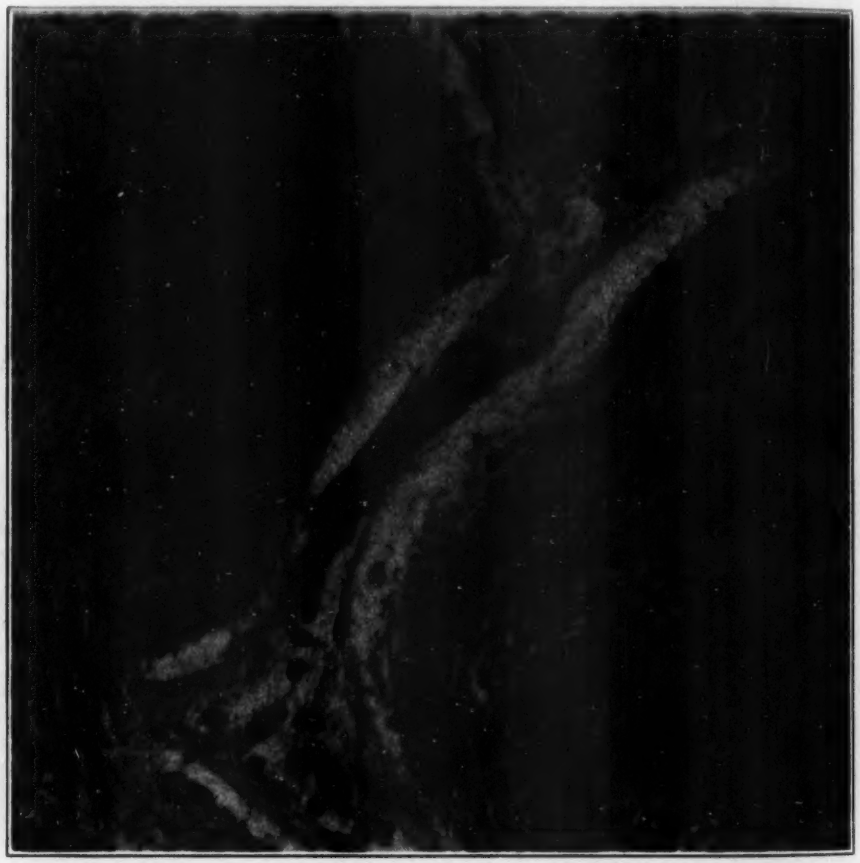

Fig. 56 (case 3).—Transverse section through the tumor of the nerve stem. Same section as in figures 53 and 55. Note the polymorphism of cells. Glial fibers can be seen surrounding nuclei of astrocytes as they pass from one funiculus to another. In these areas and also where the fibers abut the connective tissue septums the nuclei of the astrocytes become more spindle shaped.

Comment.—The varied aspects of this remarkable case deserve further comment. The early diagnosis was made possible by the fact

that I had but recently studied cases 1 and 2, operation having been performed in the latter case earlier in the same year; otherwise, the slight exophthalmos and pallor of the nerve would scarcely have justified an operation for tumor of the optic nerve. The information gained through the recent study of these cases, however, seemed to warrant exploration.

Fig. 57.—Same section as in figure 54 (phosphotungstic acid and hematoxylin stain; × 550). Note the dense glial fibers throughout the funiculi. They have also invaded the fibrous intraseptal spaces.

I excised part of the nerve, even though it showed no gross evidence of tumor formation and was apparently about of normal size, because of my convictions concerning the diagnosis.

At first no definite tumor formation was noted, although the sections were studied by a general pathologist and by an ophthalmic pathologist.

More extensive study, however, disclosed that early gliosis or gliomatosis was present throughout the nerve. An opportunity was thus afforded for study of these tumors in a very early stage of their growth.

Examination of the nerve at this time and subsequent studies throw some further light on the evolution of these growths. The tumor in this case unquestionably began as an abnormal proliferation of the

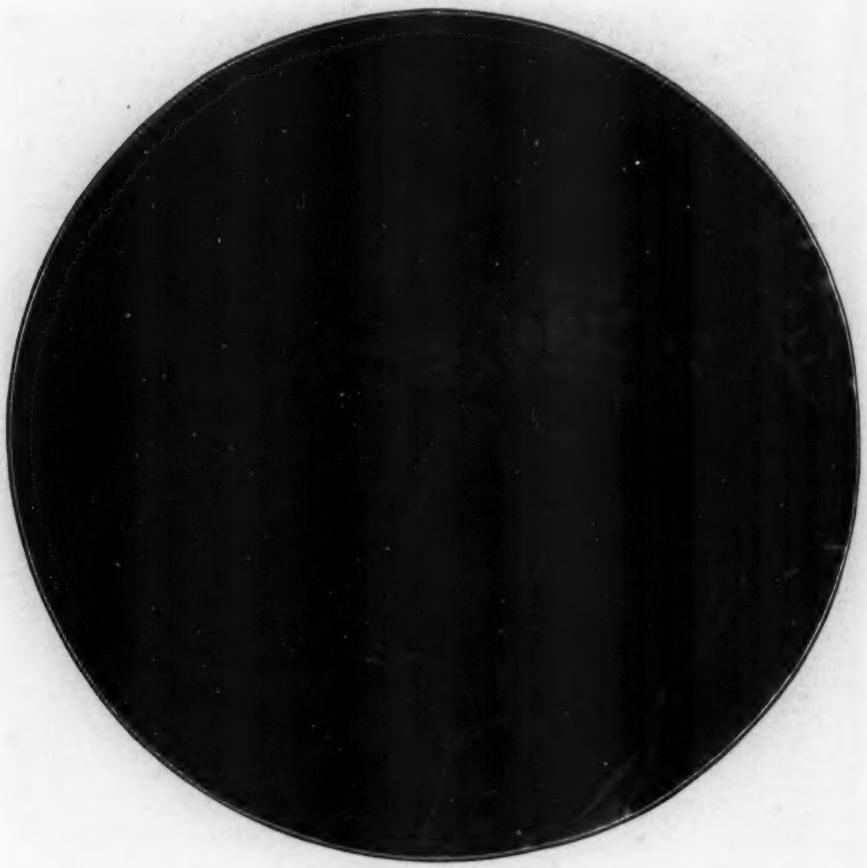

Fig. 58.—Higher power magnification of the section in figure 59. Note the glial fibers invading the pial sheath (the fibers appear black). The proliferating arachnoid cells outside this contain no glial elements. The dura is above.

neuroglial elements of the nerve stem and later spread through the pial sheath into the subarachnoid space. The proliferation of arachnoid cells was sharply defined and of such size that it appeared to be an independent growth, but it was not glial in nature. It seems more likely

that it arose as a process of reaction due to glial invasion through the pia, though it is possible that it arose through some common defect or stimulus.

The marked reduction of visual acuity and the early disappearance of the nerve fibers suggest that some degenerative change in the nerve itself may be the primary change in this disease, while glial proliferation and subsequent tumor formation may be a secondary process.

Fig. 59 (case 3).—Transverse section through the tumor (Mallory's phosphotungstic acid–hematoxylin stain). Note the glial fibers in the broken-up pial lamellae. Proliferating arachnoid cells occupy most of the subdural space the same as in figure 1.

Unfortunately only sections stained with hematoxylin and eosin, with Van Gieson's stain, with phosphotungstic acid and hematoxylin and with Weigert's methods were available for study of that portion of the nerve originally removed.

The multiplicity of the lesions, that is, the involvement of the ciliary nerves of the orbit, the nerves of the uveal tract, the gliosis in the

fellow optic nerve, the lesions in the brain and the peripheral changes would seem to furnish abundant evidence that the tumor of the optic nerve was but a part of the syndrome known as Recklinghausen's disease.

The plexiform lesions of the ciliary nerves and the early buphthalmos were not recognized clinically. A slight fulness of the upper lid fold was commented on, but the tumors of the ciliary nerves were mostly

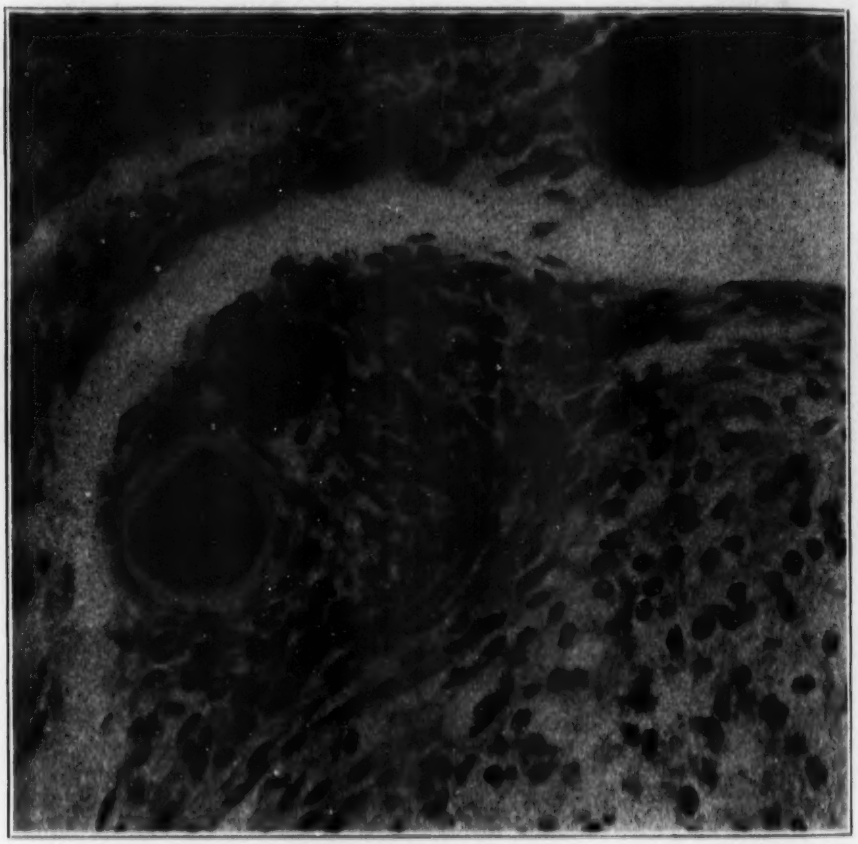

Fig. 60 (case 3).—Section showing an area of proliferated arachnoid cells in the sheath. Note the slight tendency to whorl formation surrounding a psamomma body. This was the only area in the entire tumor, however, in which there was any suggestion of "whorl" formation of cells.

microscopic in size, and no definite masses or cords could be palpated. The marked cupping of the optic nerve was repeatedly noted, but there was no other evidence of intraocular tension. The slight enlargement of the globe was noted, but its real cause was not suspected until the eye was removed. Repeated photographs showed no evidence of an

enlarged globe until the one taken just before the intracranial exploration. There was, to be sure, slight exophthalmos, which persisted after the original operation. This I attributed to possible recurrence of the growth in the unremoved portion of the nerve. It is impossible to know the exact cause. The enlarged globe, the thickened ciliary nerves and the advancing tumor of the optic nerve had all, no doubt, contributed

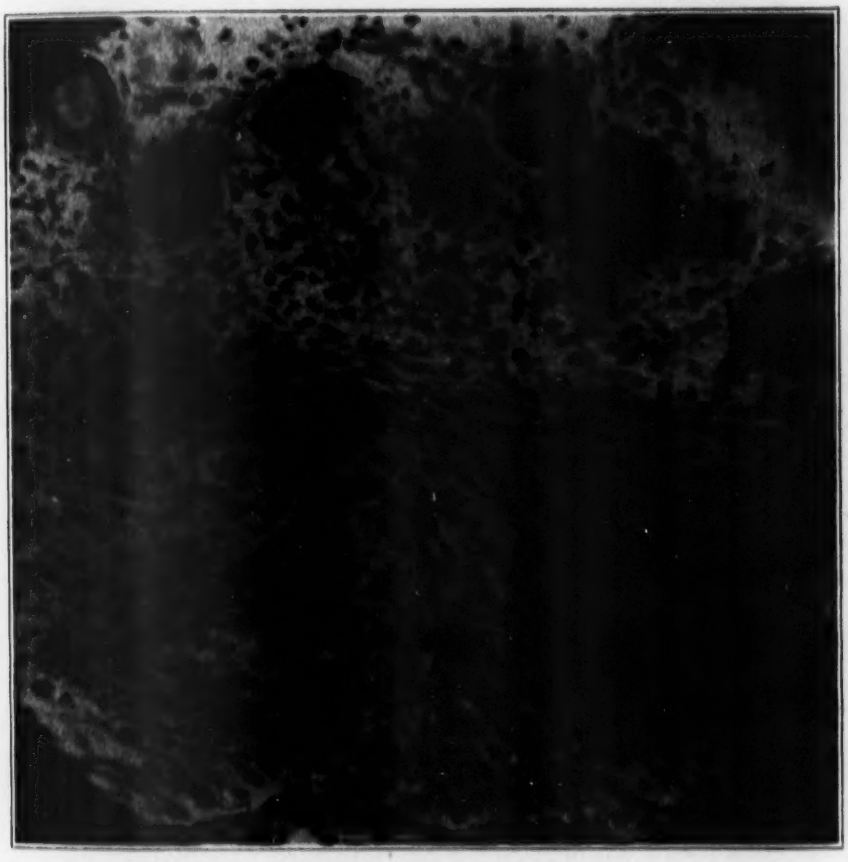

Fig. 61 (case 3).—Detail from the area of the sheath beneath the dura (hematoxylin and eosin; × 400). Note the hyperplasia of arachnoid cells with psamomma bodies.

to it. Viewed in this retrospect, it seems likely that the large and deep cupping of the nerve head was due to early glaucomatous changes, though the cornea was clear and remained so for some years after the sectioning of the nerve, and the intraocular tension never appeared to be elevated. It was taken repeatedly by touch, but owing to the child's lack of cooperation tonometric studies were not made, as this would

have required the use of a general anesthetic. The possible cause of the hydrophthalmos in these cases will be discussed elsewhere.

The roentgen studies in this case have been especially interesting. Numerous examinations were made over several years, which have permitted study of the progressive nature of the lesion. The first films showed no evidence of intracranial pressure, though later ones revealed

Fig. 62 (case 3).—A tumor developing along the course of a ciliary nerve. Normal nerve fibers are entering the tumor (hematoxylin and eosin stain).

digital impressions. The asymmetry of the orbits was present at the first examination, but its clinical significance was not recognized at the time. It has been reported by others in association with plexiform neurofibromatosis of the lid and orbit. The anterior deformity of the sella turcica was not recognized at the first reading of the films. The first films showed only the slightest sign of it, but the enlargement definitely

progressed, due, no doubt, to the increasing size of the optic nerves and consequent distention of the optic foramens or to erosion under the anterior clinoid processes.

CASE 4 (fig. 67).—*Diagnosis of early glioma of the optic nerve and chiasm, associated with the abortive type of Recklinghausen's disease; cutaneous café au lait-pigmented patches; mollusca fibrosa; transfrontal craniotomy with exploration of the region of the chiasm and optic nerve; attempted unroofing of the right optic canal; cystic glioma of the chiasm and right optic nerve, compressing the left optic nerve.*

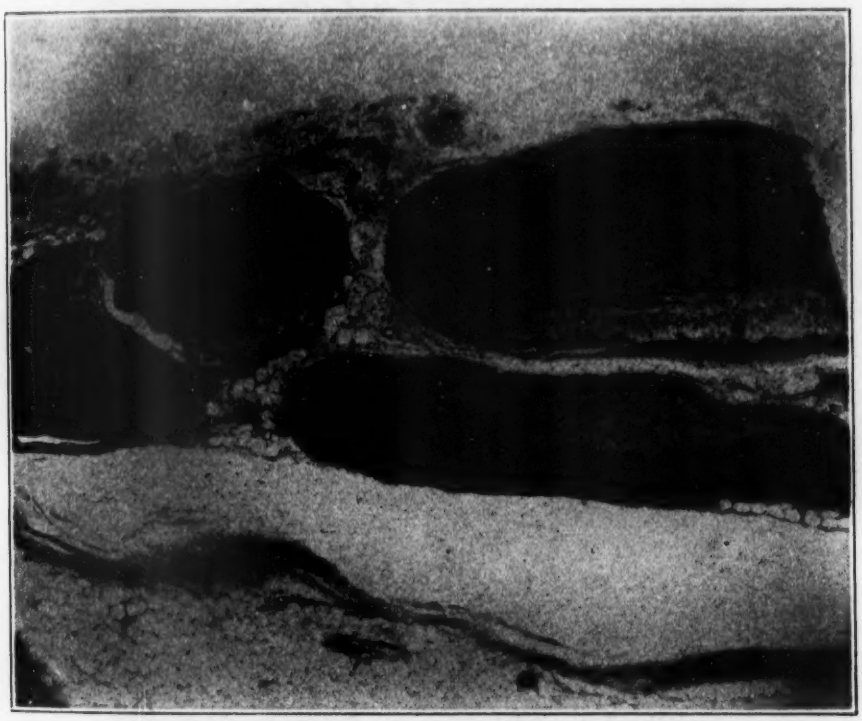

Fig. 63 (case 3).—Ciliary nerves of the orbit (Weigert stain). On the lower right side the nerve fibers have partly degenerated and are replaced by proliferation of fibrous elements of the nerve. On the upper right side a few myelinated fibers remain in the center of the proliferated nerve. On the upper left side a nerve is cut transversely, which is partly degenerated, though most of the fibers are intact. The appearance of the tumors in these nerves suggests a reaction about the nerve which has followed the disappearance of the nerve fibers.

H. L. S., a woman aged 20, was first examined by me on Nov. 30, 1938, in consultation with members of the department of medicine. Her chief complaint was of failing vision and headaches in the back of her head and neck. The patient had been referred to the outpatient service of the department of medicine because of headache and failing vision of three months' duration. She complained of recent

rapid failure of vision in her right eye and of almost daily headaches in the frontal, occipital and vertical regions. The pain in the head was mild and was usually relieved by 5 grains (0.324 Gm.) of acetylsalicylic acid. There were frequent slight nausea and occasional vomiting, which was never projectile in type. The patient's appetite was poor, and her weight had fallen from 158 pounds (71.7 Kg.) to 138 pounds (62.6 Kg.). The remainder of the history was unimportant except for menstrual irregularity, which had existed since onset, at the age of 12. The patient

Fig. 64 (case 3).—Group of nerves of the orbit near the optic nerve. The two smaller nerves show early degeneration. The large nerve at the left has completely degenerated and is jellified or liquefied. This is evidently Antoni's type B "neurinoma."

also complained of nervous irritability, worry and at times melancholia. Physical endurance was reduced, and she felt cold much of the time.

Previous Medical History.—The patient had been admitted to the medical service of the hospital six years previously, when aged 14, for a brief study. At that time she complained of headache, pain in the back of her neck and menstrual irregu-

larity, with nausea and vomiting. She was overweight and had some trouble with acne. A general examination, which included routine laboratory studies and roentgenograms of the skull and sinuses, gave essentially negative results. The sella turcica was normal. Gynecologic examination led to a diagnosis of amenorrhea on an endocrine basis, with no discoverable cause. Nothing definite could be found to account for the headaches. No ocular studies were made at this time, though the patient was subsequently studied by an ophthalmologist. Again, one and a half years prior to the present admission, an ophthalmologist studied her and found

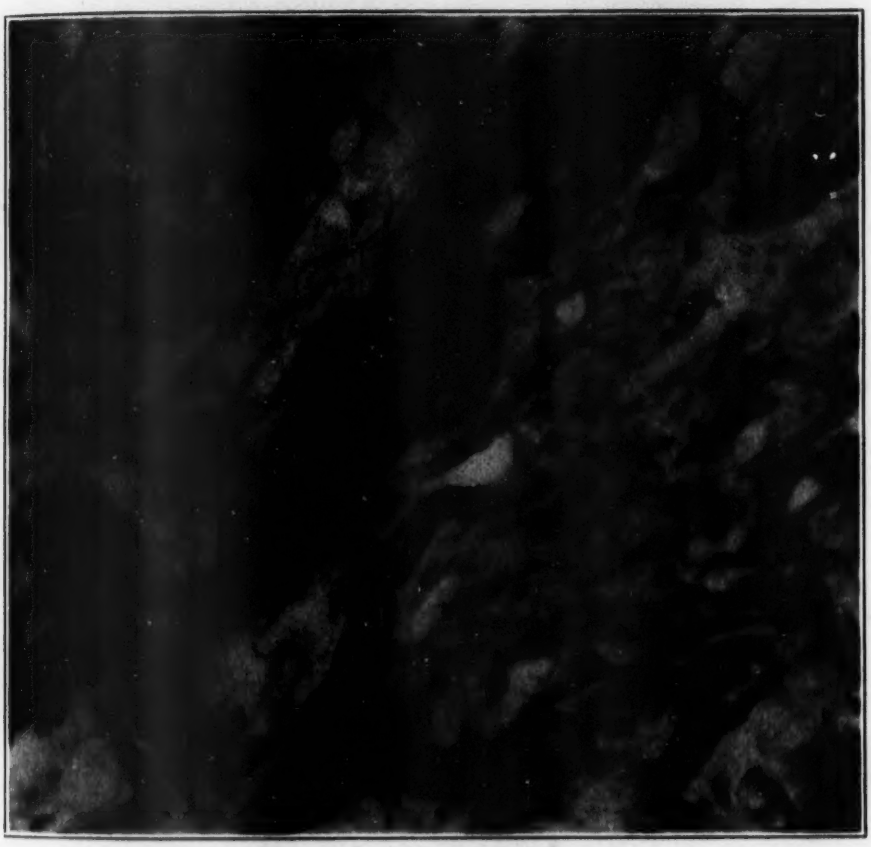

Fig. 65 (case 3).—High power magnification of a tumor similar to that in figure 64. Note the complete liquefaction or jellifaction of the tumor. Only strands of hyalinized connective tissue remain (Antoni, type B).

only a slight refractive error. She had been recently reexamined by the physician who had previously studied her eyes, and bilateral atrophy of the optic nerve with reduced fields had been noted. Since nothing was found to account for the atrophy, she had been referred to the hospital for study.

Family History.—The family history, obtained on the patient's admission, was irrelevant. Later questioning, however, revealed that the patient's paternal grandmother had lost her vision completely at the age of 78 and, further, that she had

a number of pigmented spots on the skin. The father and mother stated they had never noted any pigmented spots on their bodies, but they were not examined.

Examination of the Eyes.—Both eyes appeared normal to external examination, aside from the faintest widening of the right palpebral fissure. This was so slight that it was easily overlooked on casual inspection. Measurement with the exoph-

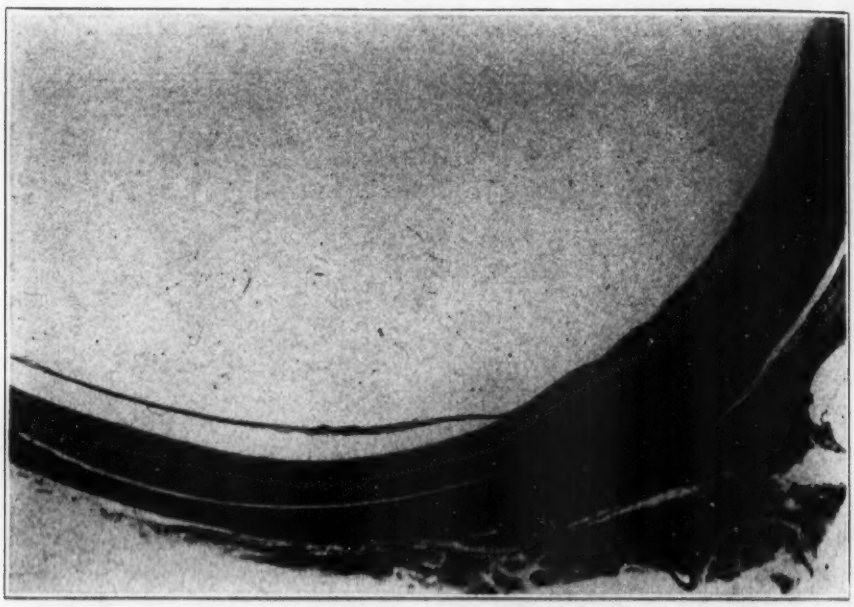

Fig. 66 (case 3).—Section through the posterior segment of the globe showing the thickened choroid. The sclera is also much thickened, and the ciliary nerves are much enlarged.

Fig. 67 (case 4).—Glioma of the chiasm and the right optic nerve. The cystic area of the tumor pressed on the left nerve. (Dilatation of the pupil of the left eye was caused by the instillation of homatropine hydrobromide.) There was slight exophthalmos of the right eye, which measured 2 mm. greater than the left eye.

thalmometer confirmed this observation, since there was an exophthalmos of 2 mm. The exophthalmometer reading was 16 mm. for the right eye and 14 mm. for the left eye. Extraocular movements were normal. The pupils were equal and reacted

normally to light and in accommodation. They dilated equally with homatropine hydrobromide. Intraocular tension was normal. Visual acuity was 20/200 in the right eye and 20/15 in the left eye.

Ophthalmoscopic examination showed that the media were clear, and the lens and vitreous appeared normal. There was bilateral atrophy of the optic nerve of about grade 2, the disk of the right eye being somewhat paler than that of the left. The disks were flat, with small central physiologic cupping. The borders were fairly sharply defined, though the superior and inferior margins were less distinct. The left disk showed a thin glial membrane in the physiologic cup which extended over the nasal border for a short distance beyond the disk. There was also a similar opaque, veil-like opacity which obscured the inferior temporal vein at a point about 2 disk diameters from the border of the disk. The retinal vessels in both eyes appeared more narrow than usual for a subject of this age. The veins were slightly tortuous.

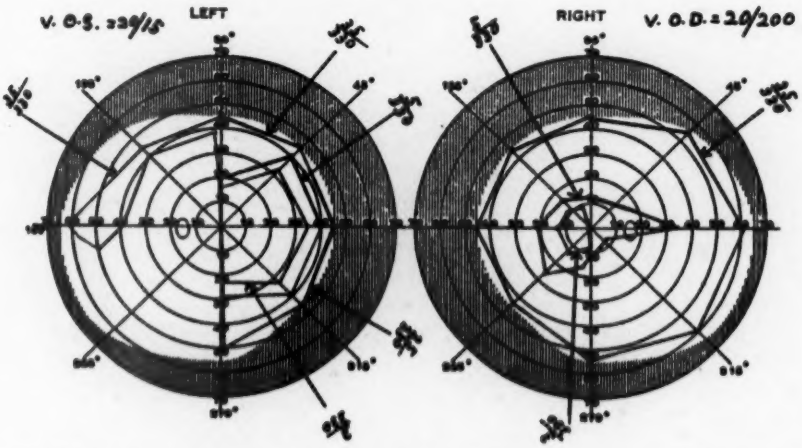

Fig. 68 (case 4).—Visual fields. There was bitemporal hemianopia, somewhat atypical though quite definite, with small test objects.

Study of the visual fields (fig. 68) revealed an atypical bitemporal hemianopia. The field of the left eye for form and colors showed a fairly typical temporal hemianopia with some added constriction in the inferior nasal quadrant. The field of the right eye was much less typical, though hemianopia was revealed with the smaller sized test objects and careful plotting. The extreme peripheral field appeared strikingly normal with a large test object, but the results of repeated tests proved somewhat variable. There was doubtful perception for color. No doubt the extremely poor visual acuity and the marked enlargement of the blindspot interfered with accurate plotting.

General Examination.—The patient was subjected to a complete examination by the department of medicine, including laboratory tests, a Wassermann test, a sugar tolerance test and roentgen examination of the skull, sinuses and optic foramens. In addition, consultations were obtained with members from the departments of surgery, gynecology and neurology. The only findings of importance were a number of light coffee-colored spots in the skin, scattered over various parts of the body. Most of these were typical smooth, nonelevated café au lait patches, such

as are frequently found in Recklinghausen's disease. (Figure 69 shows the location and size of these pigmented areas.) A typical molluscum fibrosum was found on the left breast. It was about ¼ inch (0.64 cm.) in diameter, was slightly elevated and felt soft and doughy to the touch. One other similar area was found. The left facial mimic innervation was less pronounced than the right, but voluntary facial movements were normal. There was ringing in both ears, not associated with abnormalities of the cochlear or vestibular portion of the eighth nerve. No cranial pressure points were found. Abdominal and patellar reflexes were slightly

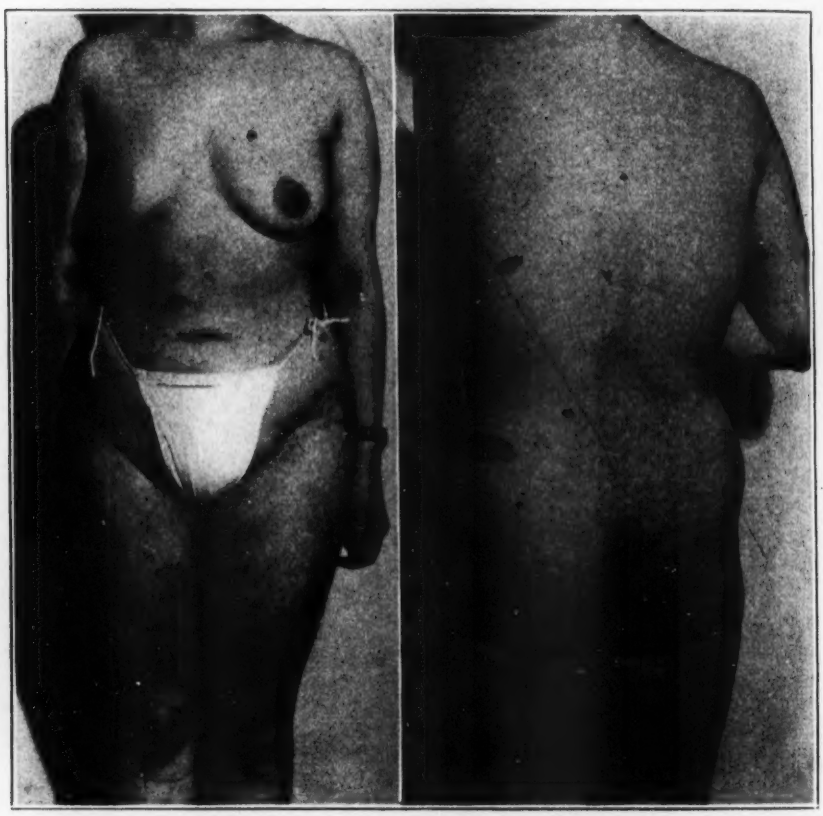

Fig. 69 (case 4).—Front and back views of the patient, showing café au lait-pigmented patches and fibromata mollusca.

decreased. Roentgenograms of the skull revealed larger and more tortuous vessels in the right frontal region than in the left. Lateral stereoscopic views of the skull showed no abnormality of the body of the sella turcica, but a shadow under the anterior clinoid process was suggestive. Views of the optic foramens showed that the right foramen was slightly larger than the left. On the films the right foramen measured 5 by 5 mm. and the left 4 by 4 mm. (fig. 70).

A diagnosis was made of Recklinghausen's disease, with early gliomatosis or glioma of the chiasm extending into the optic nerve. Intracranial exploration

was advised with a view to unroofing the bony foramens and possible incision of the sheaths of the nerves and chiasm.

Operation (Dr. W. Mck. Craig, Jan. 3, 1939).—"With the patient under intratracheal anesthesia, a right transfrontal craniotomy was performed, and the right frontal lobe was elevated. The optic nerves and chiasm were easily exposed, and a large mass could be seen within the substance of the right optic nerve (fig. 71). In dissecting the mass free, the left lateral portion was found to be cystic, and when it was punctured a yellowish fluid escaped, allowing the collapse of the mesial portion of the tumor. Because the swelling extended to the optic foramen, an attempt was made to unroof the right optic nerve. This was unsuccessful because of the vascularity of the bone and contigious tissue. The wound was closed in the usual manner."

The patient made a satisfactory postoperative recovery. A series of high voltage roentgen treatments was advised with the hope of limiting the progress of the growth.

Diagnosis.—A diagnosis was made of cystic glioma of the right optic nerve and chiasm.

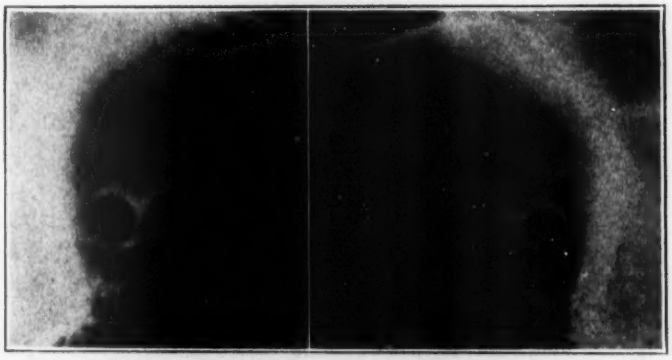

Fig. 70 (case 4).—Roentgenograms of optic foramens (actual size). Note that the foramen on the right side is slightly enlarged.

Comment.—Since the preoperative diagnosis in this case indicated a lesion of the chiasm as well as of the optic nerve, operation was advised, chiefly with a view to decompression of the nerves by removal of the roof of the bony foramens. Further, since vision was rapidly failing and blindness appeared inevitable, exploration seemed warranted.

While it was not considered wise to jeopardize the vision by removal of a section of the tumor for biopsy, there is no question that pathologic examination in this case would reveal a gliomatosis similar to that noted in the chiasm in case 3. The tumor had evidently progressed to a somewhat more advanced stage than the chiasmal lesion in case 3, since the chiasm appeared enlarged. The right nerve also appeared to be approximately twice its normal size, but the left nerve, to gross inspection, was not definitely enlarged.

The pigmented patches in the skin, with two small mollusca fibrosa, together with the atrophy of the optic nerve and a fairly typical chiasmal field change, made the diagnosis simple.

The small glial veil bordering the disk may be an early gliosis of the nerve head. The area to the inferior temporal side may also be of the same nature. A glioma of the neuroglial elements of the retina may occur, producing a true glioma of the retina, which is not to be confused with retinoblastoma or so-called glioma retinae. A tumor of this nature (astrocytoma) has been reported by McLean (1937). Later progression in these areas may throw further light on this subject.

This case again strikingly illustrates the diagnostic value of the classic signs of the mild, abortive type of Recklinghausen's disease. At

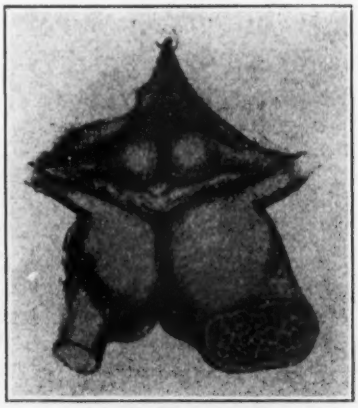

Fig. 71.—Section from a tumor described by Michel in 1873, which was also associated with Recklinghausen's disease. The specimen was similar to that found in case 4 at operation.

the original routine examination of the patient a note was made that "several cloasmas were present in the skin," but they were not considered as having any bearing on the diagnosis. Apparently general physicians have attached little or no importance to these signs, since their relation to lesions of the central nervous system which sometimes accompany them has not received general recognition.

It is my hope that this study, together with the reports cited in the literature, may in a measure aid in bringing about a better understanding of the significance of these phenomena and their importance as a diagnostic aid when associated with atrophy of the optic nerve.

CASE 5 (fig. 72).—*Diagnosis of gliosis of the optic nerves and chiasm, associated with the abortive type of Recklinghausen's disease, cutaneous café au lait–pigmented*

patches and subcutaneous neurofibromas; transfrontal craniotomy with exploration of the chiasm and optic nerves and unroofing of the right optic canal, extending into the orbital plate, followed by incision through the sheath of the optic nerve; enlargement of both optic nerves extending to the chiasm.

Mrs. R. F., a white woman aged 26, was admitted to the ophthalmic department of the Wisconsin General Hospital on Feb. 13, 1939. Her chief complaint was failing vision and headaches.

History of Present Illness.—The patient stated that her vision had been poor as long as she could remember. She recalled that she was unable to see the blackboard while sitting in the classroom when she was in grade school. She was

Fig. 72 (case 5).—Gliomatosis of both optic nerves. Note the slight bilateral exophthalmos and subcutaneous tumors of the face and cheek.

fitted with glasses at the age of 10 but noted no appreciable improvement in vision. The status of her vision remained about the same until April 1936, when it grew worse after the birth of a baby. The vision of the right eye then failed progressively for about two years, when it became stationary, while that of the left had grown gradually worse up to the time of the patient's admission. Corrected vision at that time was 20/200 in the right eye and 1/200 in the left eye. There was no history of diplopia or of inflammatory symptoms referable to the eyes. The patient complained of fairly severe headaches which were almost a daily occurrence. The headaches were worse in the morning and gradually subsided about the middle of the day. She was not nauseated at any time. She gave a history of some menstrual disturbance. There were metrorrhagia and menorrhagia.

Questioning of the patient revealed that she had always had peculiar spots on her skin (fig. 73), and she believed that these had become larger within the last few years. Cutaneous nodules had been present for about five years, and one situated beneath the surface of the skin or on the dorsal aspect of the left metacarpal bone of the thumb had been present since birth.

Previous Medical History.—In 1928 the patient suffered an injury to the hip while working in a hay field and had since had a definite left foot drop and limps with the left leg. The history aside from that related was unimportant.

Fig. 73 (case 5).—Café au lait-pigmented patches in the skin of the trunk and extremities.

Family History.—The patient stated that so far as she knew no member of her family had any serious disturbance of vision or any pigmented spots on their bodies. She made a similar statement regarding her two children, but subsequent examination revealed that 1 child, a girl of 3 years, had numerous pigmented patches in the skin distributed over various parts of her body.

Examination of Eyes.—External examination of the patient's eyes showed them to be in normal position. Extraocular movements were normal except for a slight limitation in the field of the left external rectus muscle. There was an

unsustained nystagmus when the patient looked to the right. Both eyes seemed to be somewhat prominent, and exophthalmometer measurements were 15 mm. for the right eye and 17 mm. for the left eye. There was a definite widening of the palpebral fissures which produced a starey appearance (fig. 72*A*). The pupils were equal and reacted normally to light and in accommodation.

Examination of the right eye showed a normal anterior segment. The vitreous body was clear. The nerve head showed rather advanced atrophy with a physiologic excavation and a piling up of a moderate amount of pigment about the margins of the disk. The vascular system showed moderate narrowing of the arteries and a slightly increased fulness of the veins. There were no hemorrhages. There was an occasional small deposit of pigment about the periphery of the retina. The retina itself showed numerous small areas out toward the periphery that appeared to be grayish streaks. These suggested the possibility of some glial proliferation. The macula was normal.

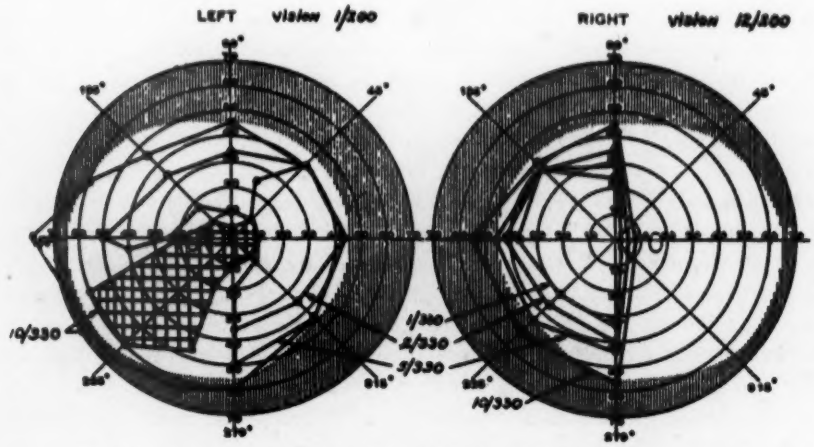

Fig. 74 (case 5).—Visual fields showing bitemporal hemianopia.

External examination of the left eye also gave negative results. The appearance of the fundus was much the same as that described for the right eye, with the exception that the atrophy of the optic nerve in this eye was much more advanced. The tension in each eye was 13 mm. (Schiötz). There was no pain on pressure over the eyeballs, but there was some pain when mild pressure was exerted over the lateral rims of each orbit. There was no fulness in the soft parts of either orbit.

Careful studies of the visual fields with a 3 mm. target revealed a bitemporal hemianopia (fig. 74). There were a central scotoma in the left field and complete loss of color perception. Visual fields obtained with various-sized targets are also shown in figure 74.

General Examination.—As far as the primary condition was concerned, the results of the general examination were essentially negative with the exception that over the entire surface of the body there were many café au lait–pigmented

spots. These varied considerably in size. There were many subcutaneous nodules, particularly over the forearms and hands.

The blood pressure was 100 systolic and 60 diastolic.

Roentgenograms of the optic foramens revealed slight bilateral enlargement, the left being larger than the right. Roentgenograms of the skull were found to be essentially normal. The sella turcica was normal in size and contour.

Laboratory examination showed nothing of especial interest. The blood chemistry was within normal limits, and the Wassermann reaction of the blood was negative.

An audiogram showed the patient to have a 15 per cent loss of hearing in the right ear and a 26 per cent loss in the left. No clinical significance was attached to this finding.

The patient was seen in consultation by Dr. H. H. Reese, of the neurologic department, who reported the following positive findings: There was a certain euphoric attitude out of proportion to the patient's disability. There was an evident facial asymmetry, a difference in the two arms and some slight alteration in the pelvis and legs, the left leg being the larger. Examination of the cranial nerves revealed weakness of the entire left seventh nerve, more marked in the oral branches. There was mild paresis of the abducens nerve on the left side. The motor strength was equal except for mild paresis of the left peroneal nerve. There was discoordination in the adiadokokinetic phenomena, with suggestion of rebound phenomena, and in the performance of hopping tests, the left leg being less efficient. Sensation for all modalities was found to be intact. Reflexes revealed a hyperactivity on the left side with a well established Babinski sign. It was the opinion of Dr. Reese that the multiplicity of findings could not be conditioned by a single lesion. He felt that there was evidence to warrant suspicion of a lesion in the right frontobasal and the left cerebellar region, plus the evident lesion in the region of the chiasm.

The patient was also seen in consultation with Dr. Robert Burns, of the orthopedic department, who found that the gait was unsteady. The left lower extremity was spastic. The left hip was high. When the patient was standing at ease, the weight was borne chiefly on the right lower extremity. There was total scoliosis with convexity to the right, which was obliterated by forward bending. Roentgenograms of the spine, of all the bones of both legs and of the pelvis revealed only the presence of scoliosis in the lumbar region with convexity to the right and small elongated cystic areas in the lower ends of both fibulas. These could not be definitely said to be evidence of involvement by neurofibromas.

A diagnosis was made of gliosis or glioma of the chiasm with extension into the optic nerves. Other lesions within the brain were considered as a distinct possibility.

Transfrontal exploration was advised, with a view to decompression of the optic nerves and possible incision of the sheaths of the nerves.

The patient was under observation for about two weeks, since she had a mild secondary anemia.

Operation (Dr. E. R. Schmidt; March 7, 1939).—Transfrontal craniotomy was performed. Exploration was carried out first on the left side, and the optic nerve was easily exposed. It was found to be more than twice its normal size,

and the sheath was smooth and tense. Similar exploration followed on the right side, and the optic nerve was found to be fully as large as the left. The roof of the bony canal and a part of the orbital plate were removed on the right side, following which an incision about ¾ inch (1.9 cm.) in length was made in the sheath of the nerve. The enlarged nerves could not be satisfactorily exposed where they joined the chiasm. Attempts to elevate the frontal lobes sufficiently to visualize the chiasm were attended by bleeding, so it was deemed unwise to proceed further in this direction. No effort was made to uncap the left nerve because of the almost total loss of vision in this eye and the added time which would have been required for this procedure.

The patient made a prompt and satisfactory postoperative recovery. No change was noted in her vision one week after operation.

Diagnosis.—A diagnosis was made of gliosis of the optic nerves and chiasm.

Comment.—The similarity of the physical findings in this case and in the preceding one is evident. That these 2 patients sought consultation about the same time is remarkable when one considers the rarity of these tumors. Since in neither case was roentgen evidence found of disease within the sella turcica, each might have been passed over for an obscure case of atrophy of the optic nerve due to retrobulbar neuritis. With the presence of the telltale signs of Recklinghausen's disease, however, as noted in the coffee-colored spots in the skin and the presence of the subcutaneous tumors, one should not long remain in doubt concerning the diagnosis.

Cushing, in his classic paper concerning the chiasmal syndrome, has so clearly presented the important features of these cases that any one who reads it should be able to make a diagnosis. Gliomas which involve the chiasm and intracranial portion of the optic nerves are less common than the intraorbital variety, as pointed out by this author. Exophthalmos is usually absent, at least for a time, unless the growth extends into, or later develops within, the orbital part of the nerve.

Changes in the visual fields of these cases are indispensable for diagnosis. The hemianopia in the less affected eye was sharply limited in this case, which, according to Cushing, is somewhat contrary to the rule. The extremely poor visual acuity in the left eye made it difficult to obtain a perfectly accurate and uniform field.

Undoubtedly the lesion of the optic nerves also involved the chiasm. The difficulties encountered in making a satisfactory exposure of the chiasm may have been due to its "post-fixed" position or possibly to the diffuse invasion of the surrounding region which prevented elevation of the frontal lobes.

(To Be Concluded)

IMPRESSION TECHNIC FOR CONTACT GLASSES

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The newer method of fitting contact glasses by a mold has superseded the previous trial and error method. The stock lenses will fit in about 25 per cent of cases. There are so many variations in the shape and size of the sclera and cornea that it is impossible for all eyes to fall into certain classifications of sizes. Perhaps in the future a testing set containing many sizes and shapes will suffice, but at present the impression and mold method is preferable.

The more impressions I make of eyes for contact glasses, the more I am convinced that a glass made from a mold of an eye is superior to a stock lens; also, that in order to have a good molded glass, it is necessary to have as good an impression as it is possible to make. The better the impression, the better the glass will fit. If the impression is not perfect, one cannot expect the manufacturer to make a good glass. Furthermore, if a technic is used which will enable changes to be made in the glasses, work with contact glasses will be more successful.

In making an impression of the cornea and the anterior part of the sclera, accuracy of the impression is of paramount importance. At best, it is possible to obtain only a poor approximation of the eye. Factors which hinder the production of a perfect negative form are: the pressure used in placing the impression material, an imperfect plastic, movement of the eye and the fact that soft, pliable tissue is being worked with rather than a solid surface.

The technic which I find gives the best scleral approximation is with the use of dental wax, such as Kerr's dental wax of gage 20. The old negocoll-hominit procedure is still the best for an impression of the cornea and the limbus.

Dental wax of gage 20 is 0.7 mm. thick. The first step is to determine the approximate scleral curve by means of a round glass of known curvature. A piece of wax 3 inches (7.5 cm.) square is cut. It is slowly molded over a hemisphere of the same radius of curvature as the sclera of the eye. Different sizes of hemispheres are used, such as 11, 11.5, 12, 12.5 and 13 mm. It is best to start with the largest size and mold the

This paper was presented as a graduate lecture at the Forty-Fourth Annual Convention of the American Academy of Ophthalmology and Otolaryngology, Chicago, Oct. 10, 1939.

wax on successively smaller hemispheres until the same radius of curvature as that of the eye is obtained. The center of the wax is then punched out with a punch 11 mm. in diameter. A glass center 12 mm. in diameter is placed over the hole and cemented with wax. Next, the overall dimensions are determined by inserting different sizes of contact glasses in the eye. I use those 20 by 22 mm., 22 by 24 mm. and 24 by 26 mm. in size. A contact glass of the chosen size is placed over the wax form, and the wax is cut around the edge of the glass. A wax form is now available with a glass center of the approximate scleral curvature of the eye and the dimensions of the desired glass. This is placed in ice water for five minutes. It is then put in the anesthetized eye for fifteen minutes, care being taken that the center of the glass is over the center of the cornea. The eye should be fixed in one position as nearly as possible for fifteen minutes. The form is then sprayed with ice water to harden it. A rubber sucker is applied to the glass center, care being taken that in removal the form does not touch the lids. If it does, the impression will be incorrect. The form is placed in ice water, and preparations are undertaken to make the positive form.

This is made of dental stone. By practice, one can learn the proper proportions of powdered stone and water to be used. The mixture of stone is placed in the wax mold; an additional stone mixture is placed into a mold, and the wax is inverted over the mold filled with stone until it hardens. After it is hard, the wax is trimmed away and the positive form is completed.

A skeleton glass is made from this form. Often the glasses as received from the manufacturer are not a perfect fit, even though they may be a close approximation of the cast of the eye. The reason for this is the impossibility of making an exact impression of an eye, as stated previously. Therefore, it is well to use a glass which can be corrected or, if necessary, to have a new glass made which will incorporate any necessary changes. The fitting of the glass to the eye is the difficult part of contact glass work, and it requires much time and patience, both on the part of the examiner and on the part of the patient. It is better to make the first observation of a glass without any solution in the anesthetized eye. Various points are noted. The overall size is of first importance. It must be large enough to cover a wide area of sclera without going into the lower fornix or onto the semilunar fold. The convexity and depth of the glass are noted. A glass should be just deep enough to clear the cornea. Naturally, it must not rub over the cornea, and it must not be too deep or there will be a sliding of the glass over other parts of the cornea or limbus when the eye is moved. Finally, the limbic area is watched for pressure and sliding. The glass is removed, and 3 drops of fluorescein is placed in the bowl, which is then filled

with saline solution and reinserted. Now, areas of contact will be shown, and the glass should be looked at with the slit lamp. If the glass contacts at forbidden areas, these places are marked on the glass and on a plaster of paris copy of the glass and returned to the manufacturer for correction.

If the glass looks good in the eye, it is removed and reinserted with physiologic solution of sodium chloride and worn for a four hour testing period. If the glass can be worn comfortably for two four hour periods without causing any corneal abrasions or air bubbles, it is ready for optical grinding. If it causes burning, tearing or redness, obviously the fit is incorrect. The formation of air bubbles is a frequent and annoying occurrence. They are due to a glass being of too great or too little convexity. An aid in finding the point of entrance of air is to place a drop of fluorescein at the edge of the glass and to watch its entrance into the bowl of the glass. A yellow channel may be seen, indicating the point of entrance of air.

When it is determined that the skeleton glass is correct, a finished glass is made with the proper optical correction. To arrive at the proper corneal prescription, it is necessary to have only a few afocal test glasses of known radius of curvature, such as 8, 8.5 and 9 mm. Ordinary lenses from the trial case can then be added in a trial frame to obtain the desired vision, and the distance between the contact glass and the auxiliary lens measured.

The best solution to use is physiologic solution of sodium chloride buffered with sodium bicarbonate. After considerable experimental work, I have come to the conclusion that there is no value in having a solution which will conform to the p_H index of the patients' tears. If a contact glass causes redness, tearing, or discomfort, it is because it is ill fitting, and although a solution of a different p_H index might give temporary relief, there can be no lasting benefit. If a contact glass causes untoward reactions, there is probably pressure at the limbus or on the cornea.

Requisitions for a good fitting contact glass are the following: It must be the proper size so that it covers a large area without any pressure on the peripheral portion. It must not be in contact with the cornea or limbus. It must not ride or rub over the cornea or limbus when the eye is moved. Air bubbles must not form under the glass. The glass must not cause the formation of corneal abrasions. It must be worn for four hour trial periods with comfort on two successive days. The optical correction must give the desired vision. Only when these requisites are fulfilled can a contact glass be called satisfactory.

VORTEX-SHAPED DYSTROPHY OF THE CORNEA

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In 1910 Fleischer[1] described the eyes of a 37 year old woman suffering from multiple sclerosis in an article entitled "A Peculiar Previously Unknown Opacity of the Cornea." The left amblyopic eye of this patient showed convergent strabismus. Refraction of both eyes revealed high hyperopia with considerable astigmatism at an oblique axis. The corneas showed identical changes. In the superficial layers there was a fine opacity covering the whole cornea. It consisted of rays or bundles converging toward a point slightly below the center of the cornea or radiating from that point toward the periphery, like a crown of human hair. The lower and upper halves of the cornea were separated by a narrow horizontal stripe of clear corneal tissue. Higher magnification showed that the opacity consisted of small yellowish brown points and spots and that the picture of the vortex figures was caused by clear spaces between these spots. The surface of the cornea was clear and smooth. One and a half years later the condition was not changed.

In 1930 Lutz[2] reported a similar condition in a mother and her daughter. A 26 year old woman came under his observation with acute conjunctival inflammation due to hair dye. A fine, almost identical corneal opacity was observed in each eye which consisted of stripes of yellowish brown spots, converging toward the center of the cornea, where they formed a whirlpool-like figure. These stripes were broader on the periphery than in the center; they gave a scalloped appearance and were partly interrupted by clear tissue. Occasionally two or three peripheral stripes joined into one. Lutz located the opacity on Bowman's membrane or in the superficial layers of the substantia propria in a plane parallel to the surface. The vision in both eyes was 5/6. The Javal ophthalmometer showed 1.5 D. of astigmatism. The refraction was not given. The corneal sensibility was normal. The 53 year old mother of this patient showed the same changes in her corneas. After correction of hyperopia of + 2 D., vision was normal in both eyes; otherwise the eyes showed no pathologic changes.

From the service of Dr. Webb W. Weeks, Beth Israel Hospital.

1. Fleischer, B.: Arch. f. Ophth. **77**:136, 1910.
2. Lutz, A.: Arch. f. Ophth. **123**:704, 1930.

In 1931 Vogels [3] contributed an additional case. A 60 year old woman had a veil-like opacity in both eyes. Slit lamp examination proved the corneal surface to be smooth and shiny. Fine yellowish brown particles formed a whirlpool-like or vortex-like figure, terminating or beginning slightly eccentrically. The whirlpool in the right cornea was more temporally from the center and in the middle line. Fine radial stripes started from this center and widened toward the corneal margin, similarly to the tail of a comet. Between these stripes was a zone of clear corneal tissue.

REPORT OF A CASE

M. G., a 16 year old white girl, had had the usual diseases of childhood and had been seriously ill with infectious mononucleosis two years before the present examination. She had been wearing glasses for the past ten years, the last change having been made one year previously. The family history did not reveal any malformation or any hereditary disease of the eyes. The general examination gave negative results.

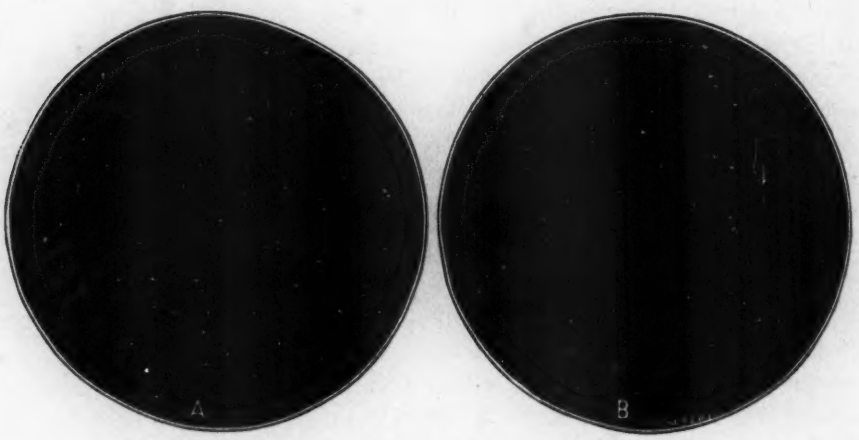

Fig. 1.—Appearance of the right (*A*) and left (*B*) corneas.

Ocular examination showed the palpebral fissures of both eyes to be equal. The lids were normal. There was no exophthalmos or enophthalmos. The ocular movements were normal, and there was no nystagmus. The conjunctiva of each eye was not injected, and there was no ciliary injection. Focal illumination revealed a fine opacity in each cornea. Irregular stripes of opaque corneal tissue started on the periphery and joined in a whirlpool slightly below and nasally from the middle of the cornea. Slit lamp examination showed that these opacities consisted of yellowish brown spots. They were located in the deepest layers of the epithelium and could not be seen underneath Bowman's membrane with the highest magnifications. The stripes were separated by channels of absolutely clear corneal tissue. The deeper layers of the cornea were normal. There were no keratitic precipitates. The corneal sensitivity was normal. The irides were brown and of normal structure.

3. Vogels, A.: Klin. Monatsbl. f. Augenh. **86**:591, 1931.

The pupils were round and equal and reacted to light and in convergence. The lenses did not show any opacities. The media were clear. The fundi showed marked tortuosity of the vessels; the margins of the disks were not sharply defined (pseudo neuritis optica). The vision was 20/80 in both eyes; with a + 5.0 cyl., axis 85 it was 20/20 in the right eye and with a + 4.5 cyl., axis 85 it was 20/35 in the left eye. The visual fields were normal. Tension in both eyes was 18 mm. of mercury (Schiötz). Examination of several members of the family did not show any similar findings.

COMMENT

Comparison of the findings in this case with those in the previously cited cases leaves no doubt that I was dealing with the same clinical entity which Duke-Elder [4] called "rare and peculiar." It is only natural that the mechanism of origin raises considerable speculation. Fleischer [1] left open the question whether he was dealing with a congenital anomaly, remnants of previous inflammations or deposits of special substances. He doubted whether it would be possible to draw general conclusions about the circulation of the normal cornea. Lutz [2] was much more positive in evaluating his observations. In spite of the fact that he found identical conditions in a mother and her daughter, making a hereditary anomaly more than probable, he believed the vortex-shaped dystrophy to be caused by inflammatory processes. He referred to Holmes-Spicer,[5] who drew attention to the fact that the spokelike opacity of the cornea could be formed by edema of the parenchyma. In one of Holmes-Spicer's cases of iritis rheumatica, the opacity extended from the limbus to the center of the cornea, like the spokes of a wheel, but disappeared after three weeks of treatment without leaving any marks. Similar observations were published by Giri,[6] Blatt [7] and Hartmann.[8] All dealt with a spokelike opacity during acute inflammation which cleared up completely after healing of the underlying pathologic process. Lutz, after an extensive discussion of the literature about the fluid metabolism of the cornea, came to the conclusion that in all these cases one is dealing with preformed channels of mechanical filtration which originate at the limbus and flow into the anterior chamber. He assumed that the same system is present in the normal eye, the normal closure of the lid furnishing the motor power for this flow.

Vogels [3] came to the conclusion, with which I am inclined to agree, that she was dealing with a special type of a rare corneal dystrophy. The lack of any signs of inflammation, the course of the disease and

4. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2.

5. Holmes-Spicer, R. L.: Roy. London Ophth. Hosp. Rep. **14**:347, 1896.

6. Giri, D. V.: Tr. Ophth. Soc. U. Kingdom **39**:145, 1919.

7. Blatt, N.: Klin. Monatsbl. f. Augenh. **80**:472, 1928.

8. Hartmann, E.: Ann. d'ocul. **161**:161, 1924.

the factor of heredity made such a diagnosis more than probable to her. She considered the peculiar whirlpool-like formation a complete riddle and declined to make any speculative, far reaching conclusions. On the other hand, she tried to clear up the question as to the nature of the pigment. Biopsy of a small piece of the superficial corneal layers led to the conclusion that she was dealing with glycogen, because there were light-diffracting droplets below the epithelium. After staining a section with compound solution of iodine, she found brownish granules. Another section, stained with this solution after extensive watering, did not show any staining.

I do not believe that Vogel's conclusions with regard to the glycogen are convincing. The light-diffracting droplets could have been one of several chemical components, and the granules stained with compound solution of iodine looked to me like the unstained original yellowish brown spots, which were removed mechanically through the intensive watering of the second specimen. Glycogen would be an extremely unusual substance to find in corneal tissue. It is the unutilized storage form of carbohydrates for a metabolic activity which does not exist in the cornea, according to present knowledge. The only place in the eye where glycogen has been reported is the myoid part of the retina, and this was doubted by such an expert in glycogen as Best.[9] Unusual collections of glycogen appear in a rare metabolic disturbance, which is called Gierke's disease. Apparently none of the patients in the previously reported cases and definitely not my patient was afflicted with the disease. Therefore I came to the conclusion that the yellowish brown spots must be some other substance. I am of the opinion that they are melanin, a brown or black pigment which occurs normally and pathologically in the ocular tissues. Melanin is a near relation to epinephrine, and in 1913 Masson [10] demonstrated the colorless mother substance of melanoblastic cells in the normal conjunctiva. Through silver impregnation they became oxidized into melanin. In 1922 Redslob [11] proved the deeper cells of the limbal conjunctiva to be potential menoblasts. They can be converted into melanin through some oxidizing ferments, the so-called dopa reaction. That this process is occasionally reversible can be proved through the following casual observation.

In 1934 a Negro came under my observation for a slight acid burn of his right conjunctiva. The limbus conjunctivae of both eyes was surrounded by a large girdle of pigment. In his right cornea an oval-shaped dense patch of brown pigment stretched for 3 mm. at 11 o'clock toward the center. The pigment was located apparently just above Bowman's membrane. Even though the acute

9. Best, F.: Centralbl. f. allg. Path. u. path. Anat. **18**:465, 1907.
10. Masson: Compt. rend. Soc. de biol. **75**:210, 1913.
11. Redslob, E.: Ann. d'ocul. **159**:523, 1922.

inflammation cleared up after a few weeks and the eyes were found to be normal, I had occasion to reexamine him at certain intervals, for the last time in August 1939. I then found that the brown path had become channeled by clear intervals, beginning at the central part of it and not yet reaching the limbus corneae at any point.

This observation gives a clue to the origin of the whirlpool-like opacity in my case. One may assume that originally a sheet of melanin granules covered Bowman's membrane and that some unknown agent

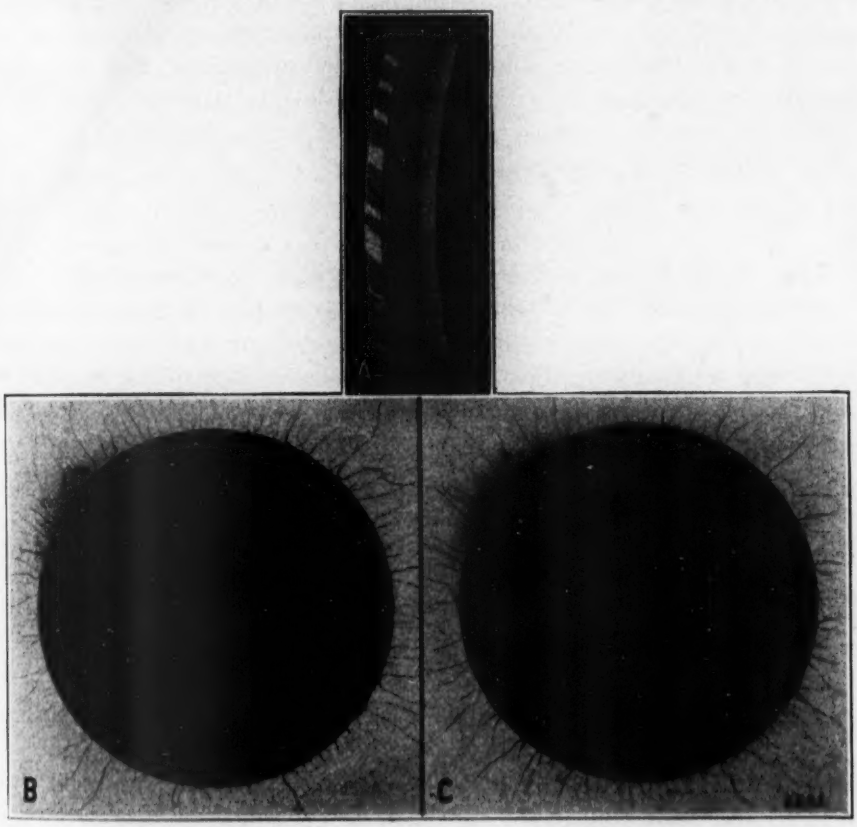

Fig. 2.—*A*, section of the right cornea as seen through the slit lamp. *B*, appearance of the right cornea in 1935. *C*, appearance of the right cornea in 1939.

filtering from the anterior chamber formed the clear channels either by dissolving the melanin or by converting it into its colorless mother substance. The picture of the upper half of the left cornea in my case makes this explanation plausible.

It seems to me difficult to explain the whirlpool-like formation of these channels. Looking for analogous formations in other parts of the human body, I find the crown of human hair and the lines of the

finger tips in similar arrangements. In the skull and in the finger tips, skin covers a dome-shaped structure; in the latter, this structure consists of muscles, and in the former, of bones. I believe that a similar arrangement exists in the cornea, the dome-shaped structure being represented by stroma covered with epithelium. It has been known for a long time that many organs, like the spongiosa of the head of the femur or the aorta, have a definite functional structure, obeying mathematical laws of mechanics. In 1935 Kokott [12] established the fact that such a functional structure exists in the sclera. One may assume that a similar structure exists in the cornea to maintain equal refraction in spite of the continuous fluctuation of the intraocular tension. The pathologic impregnation with pigment made this structure visible. It would be desirable to prove the existence of such a functional structure experimentally and mathematically.

SUMMARY

For the first time in the English-American literature a case of the "rare and peculiar" vortex-shaped corneal dystrophy has been described. As in the 4 previously reported cases, the patient was a woman with hyperopic astigmatism. In my opinion, the colored material is melanin, and the whirlpool-like arrangement is caused by the functional structure of the corneal tissue.

12. Kokott, W.: Klin. Monatsbl. f. Augenh. **94**:33, 1935.

POSTSCRIPT ON IMAGE EXPANSION BY THE FOVEAL CLIVUS

GORDON L. WALLS, Sc.D.
DETROIT

I recently demonstrated the untenability of the usual explanation of the foveal depression,[1] which holds the latter to be simply an excavation of tissue which would interfere with optimal function of the macular center as a region of maximal resolving power. It was suggested that the purpose of the depression, at least where it is deep and convexiclivate, as in Sauropsida, is to expand the image locally by a peripheral refraction of the eikonogenic rays where they strike the internal limiting membrane along the clival surfaces.

At the time, I had only logical grounds for believing the refractive index of the retina to be higher than that of the vitreous—a prerequisite for the postulated magnifying action of the foveal pit—and was unaware that actual measurements of retinal indexes had long since been made by Valentin.[2]

Valentin admonished against ignoring the disparity of the retinal and vitreous refractive indexes in fine calculations and against treating the intraocular course of light rays as if they stopped at the internal limiting membrane. He did not suggest any possible effects of the disparity, however.

Matthiessen [3] knew of Valentin's determinations (though he sadly misquotes them) and stated that while he was able to confirm them they "have no significance for dioptrics." It was perhaps Matthiessen's authority which kept the data from being perpetuated into modern textbooks.

Valentin measured the refractive indexes of the retinas of a number of vertebrates, including 6 mammals, for which the values ranged from 1.3407 for the green monkey to 1.3460 for the dog, the average for the

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From the Ophthalmic Research Laboratory, Wayne University College of Medicine.

1. Walls, G. L.: Significance of the Foveal Depression, Arch. Ophth. **18**: 912 (Dec.) 1937.

2. Valentin, G.: Ein Beitrag zur Kenntnis der Brechungsverhältnisse der Thiergewebe, Arch. f. d. ges. Physiol. **19**:78, 1879; Fortgesetzte Untersuchungen über die Brechungsverhältnisse der Thiergewebe, ibid. **20**:283, 1879.

3. Matthiessen, L.: Die neueren Fortschritte in unserer Kenntnis von den optischen Baue des Auges der Wirbeltiere, in Festschrift zur Feier des siebzigsten Geburtstages von Hermann von Helmholtz, Leipzig, L. Voss, 1891, p. 51.

mammals being 1.34385. The values for 4 and 7 month human fetuses averaged 1.3486; but it is probable that the value for the adult human being is lower, since during development in the chick the index sinks from 1.3476 (average for 12, 14 and 16 day embryos) to 1.3461 for the young adult. The average for the 2 primates studied, the green monkey and the baboon, was 1.34265, and the index for the adult human being may prove to be close to this.

Rather higher values are found for animals other than mammals. The maximum found by Valentin was 1.3794 for a frog (Rana esculenta), freshly caught in May. A specimen caught in October gave a much lower figure, 1.3416. The diet, especially its fat content, may have a considerable influence, and experiments to test this possibility would be most interesting.

The important figures for consideration here are those for the only foveate bird examined by Valentin, a species of parrot (Chrysotus aestiva). The retina of this form has an index of 1.3475; the vitreous, an index of 1.3391. By substituting these values in the computations based on figure 6 in the exposition of my theory,[1] angle *BAC* proves to be 1.64 degrees, which would afford an areal expansion of the image in the middle of the hawk's fovea of approximately 30 per cent.

The attendant local increase in resolving power appears adequate to make the magnification of the image by the clival surface of the foveal pit seem a sufficient teleologic reason for the existence of the pit, at least when it is shaped as it is in most birds and lizards.

In the concaviclivate human fovea, however, the much less precipitous clival slope and the presumptive lower refractive index would appear to make for a degree of image expansion too low to account for the evolution of the human foveal pit from no depression at all *directly* to its present gentle profile. Wherever the foveas of animals approach the fovea of man in shallowness, they can invariably be shown to have been deeper in the ancestors. In the light of the resurrected data of Valentin, it seems more likely than ever that the human fovea has degenerated, like that of Sphenodon, the owls and the pigeon,[1] from a once much more deep and abrupt depression. The possibility that the higher apes have less gradual foveas than man seems fairly strong, and it is to be hoped that studies of them may soon be made.

Many a primate has a more "diurnal" eye than man, with higher cone to rod ratios; and since retinal adaptations for diurnality and for visual acuity go hand in hand, it should not be surprising if some other primates prove to have better foveas than even the phenomenally sharp-sighted Hottentot.

OPERATION ON THE OCULAR MUSCLES

A FEW POINTS IN OPERATIVE TECHNIC

MOSES FREIBERGER, M.D.
NEW YORK

Simple modifications of the technic of operations on the ocular muscles, I have found, can materially improve the results obtained and reduce the time required. I report these for what they may be worth to others. The points made may appear simple and obvious, but they represent thought and experience, and a trial will prove their value. I am aware of the many operations on the ocular muscles, and I have found procedures of merit in many of them.

When Jameson [1] introduced his epoch-making recession operation, supplementing simple tenotomy, there grew up a literature on various modifications of this technic. Each writer described what he regarded as a simpler method of executing the essential principle of reattaching the cut muscle at a given point on the globe. These modifications are welcome additions, for in each case one may find points of value.

In 1933 Curdy [2] introduced a simplified technic for muscle recession. He advised a horizontal conjunctival incision instead of the vertical one and attachment of the muscle to the sclera with a single suture. I had anticipated Curdy's work and in the fall of 1932 had presented a similar operation at a monthly staff meeting at the New York Ophthalmic Hospital.

The technic of this recession operation as I have performed it is as follows: The conjunctival incision is made horizontally, extending from near the limbus at the 180 degree axis back to the plica semilunaris and somewhat beneath it. One of the advantages of a horizontal incision over a vertical one is that less bleeding is encountered owing to the fact that the incision runs parallel to the conjunctival vessels and that one can often avoid the vessels by cutting between them. Another advantage is the inconspicuous scar resulting. I find that frequently after healing it is almost impossible to detect the site of the incision. In making the incision, the legs of the open forceps should be placed in the direction in which the line of incision is to be made (fig. 1), so that in closing them a vertical fold of conjunctiva is grasped and readily nicked in the horizontal direction desired.

1. Jameson, P. C.: Arch. Ophth. **51**:421 (Sept.) 1922.
2. Curdy, R. J.: Am. J. Ophth. **16**:890 (Oct.) 1933.

The conjunctiva is now undermined well back over the muscle and toward the cornea. Tenon's capsule is buttonholed, and the muscle forceps is slipped under the tendon immediately behind the insertion in the usual manner. The muscle forceps is placed in position to grasp the well spread muscle. To facilitate this procedure, it is well to hold the female blade of the forceps alone and pass it beneath the muscle. This is as simple as inserting a muscle hook. After the tendon is cut, it is wise to pass the muscle hook all around the area of the insertion to make sure that no strands of muscle are still attached to the sclera. Any such strands left intact might cause failure of the operation.

A single-armed suture of no. 1 silk or 000 catgut enters the conjunctival wound from above and close to the plica. The assistant holds the conjunctiva aside while the surgeon grasps the muscle forceps and

Fig. 1.—The open forceps in relation to the line of incision.

passes the suture through the muscle from above. The suture should be so placed that it will hold a bit more than its middle third. The surgeon then allows the assistant to hold the muscle forceps while he grasps the stump with the fixation forceps to steady the globe.

The distance back on the sclera that the muscle must be receded is now noted. At this point the needle enters the superficial layer of the sclera in a vertical direction. The fixation forceps is then removed from the stump, the muscle forceps is held by the surgeon and the suture is continued through the muscle from its undersurface outward and on through the conjunctival wound opposite the initial puncture. When this suture is tied, not too tightly, it holds the muscle in place at its new insertion. It also closes the posterior end of the conjunctival wound. One or two additional sutures are usually required to close the wound completely (fig. 2).

Some doubt was raised when I first introduced this operation as to whether a single scleral bite is sufficient to hold the muscle to the sclera and whether the muscle would be spread sufficiently without additional sutures. I tried to satisfy myself and others on these points when I had occasion to do this operation on an old blind eye that was enucleated two weeks later. My patient consented to have me enucleate his eye in "two stages." At the time of the enucleation I allowed a goodly portion of the receded muscle to come away with the globe. I was able to demonstrate how well spread the muscle was at its attachment to the globe and, above

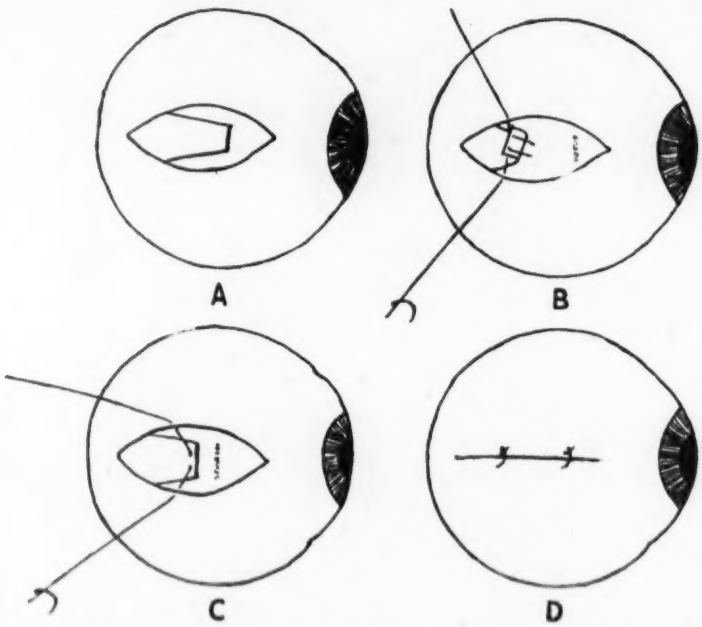


Fig. 2.—Diagrammatic representation of operative technic. In *A*, a horizontal incision (oval conjunctival wound) is made, exposing the sclera and the muscle. In *B*, the muscle is cut away from its insertion. The suture is placed in the conjunctiva, muscle and sclera, back to the muscle and out through the conjunctiva. In *C*, the muscle is resting on the sclera at its new attachment, with a single suture holding it firmly in place. In *D*, the suture is tied, uniting the margins of the conjunctiva and closing the wound. An additional suture is usually required to close the wound completely.

all, how firmly adherent it was. It required considerable power to pull it away from the sclera.

An outstanding feature of the operation is that it necessitates only one suture through the sclera. This is a distinct advantage. The entire operation is easily performed, and the time consumed is reduced to a minimum. Since 1932 my associates and I have performed over 300

recessions by this method. In view of the ease of execution, the minimum consumption of time and the good results, it must be acknowledged that this operation has merit.

With reference to the suture material used at operations on muscles, I make it a rule to use catgut in children under 8 years of age and silk in older patients. The sutures themselves are seldom longer than 6 inches (15 cm.) and at this length are easily handled and their exposure to contamination minimized. With reference to tying the sutures with

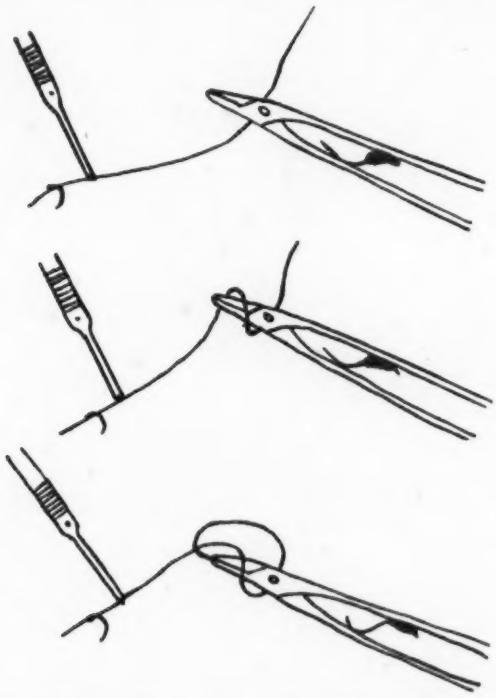


Fig. 3.—Steps in tying sutures with instruments.

instruments, I feel that this simple procedure should hardly be called to the attention of the ocular surgeon, but from frequent observation I have found that it is often done incorrectly. Figure 3 shows in a diagrammatic manner the steps, beginning with the placing of the needle holder between the short and the long end of the suture and not from the outer side of the long end. The short end need not be more than 1 or 1½ inches (2.5 or 3.8 cm.) from the wound. The long end should be grasped by the tissue forceps and wound once around the head of the needle holder; then the needle holder grasps the end of the short arm, pulls it through the loop and completes the knot. The second tie is carried out in the same manner.

For the resection operation, the method of Reese has been a standard procedure and is still popular. This operation, however, has some shortcomings which pave the way for improved technic. For example, the central double-armed suture, in passing over the muscle end and under the stump, must necessarily lie between the edge of the muscle and the stump when these structures are brought end to end. The interposition of the suture does not allow a close approximation of the muscle and stump. After all sutures are tied, there is a boggy mass of tissue due to the inclusion of excess conjunctiva, muscle and stump in the suture. The end result is a heavy, prominent scar.

I have modified the technic in my work. I use the same suture material as in the Reese operation. For the central double-armed suture, I use no. 3 braided silk, and for the lateral sutures, no. 1 braided silk. The conjunctival incision is made in the usual vertical direction and the posterior flap undermined. It is here that care must be exercised not to dissect the posterior flap too extensively, for this would have the effect

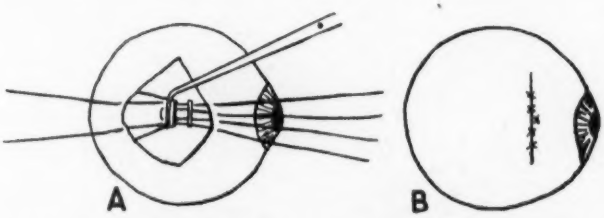


Fig. 4.—*A*, diagrammatic drawing showing the position of the sutures at the resection operation. *B*, location of the sutures after closure of the wound.

of a sliding flap, which would cause the massing of an excess conjunctiva and overlapping of the edges when the wound is closed. The flap should be dissected only over the area of the muscle and down its edges, so that the muscle alone is freed from its adjacent tissues. The anterior flap needs no undermining.

The muscle thus isolated is held on a muscle forceps while the desired portion is resected. The central double-armed suture is inserted in its middle third. The suture is introduced from above and does not include the conjunctiva. It is then continued through the middle third of the stump, on through the anterior conjunctival flap close to its margin, there to be tied later. The marginal sutures are passed in the same manner as in the Reese operation and include the conjunctival margin of the posterior flap, but the sutures should not be separated more than the width of the muscle (fig. 4 *A*).

While the assistant holds both marginal sutures, which tends to pull the eyeball forward, the surgeon ties the middle suture by hand, keeping the index fingers close to the knot so as to minimize the danger of tear-

ing the suture. The tying of this suture draws the muscle and stump together and approximates their edges. The marginal sutures are now tied. They reenforce the central suture and at the same time approximate the adjacent conjunctival margins. Two additional sutures of no. 1 silk may be required, one on either side, to close the wound completely (fig. 4 *B*). Any small areas of gaping conjunctiva between these sutures can be cemented by pinching them with the tissue forceps.

The modified technics described herein have been used by my associates and by myself on many occasions and have invariably given such satisfaction that I felt they had sufficient merit to warrant their description.

Clinical Notes

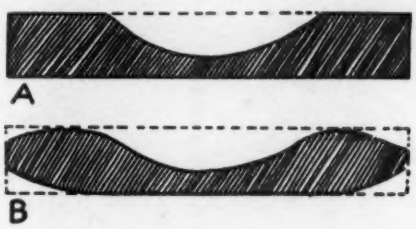
A NEW LENS

ANDREW HUNTER, M.D., McKEESPORT, PA.

A new lens is here presented which will overcome the objections to the appearance of strong concave lenses and especially do away with the sharp line which marks the periphery of the concave part of the myodisk lens.

This lens is similar to the myodisk lens, but the sharp edge of the concave part of the latter, which is so conspicuous, is replaced by a gradual curve. The margin of the lens is also cut down by a gradual curve to the thickness which is suitable for rimless mountings.

Possibly originality may not be claimed for cutting down the periphery of these concave lenses, as others may have done some work



A, cross section of the myodisk lens. *B*, cross section of the new lens.

in that direction. The distinctive feature of the lens is that the sharp edge of the myodisk lens is cut down and is replaced with a gradual curve which is not so conspicuous. The accompanying diagram shows cross sections of both lenses.

Representatives of two leading optical houses have stated that such a lens is not practicable, but patients seeking cosmetic improvement seem to like it.

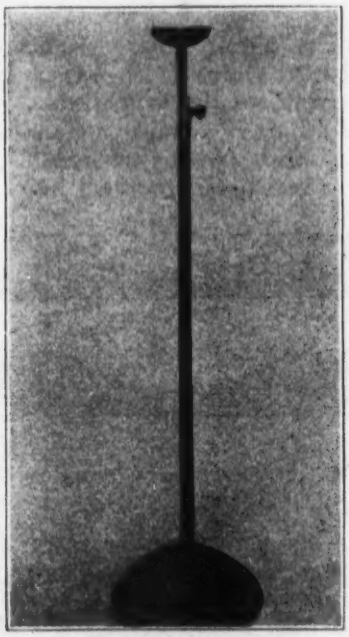
These lenses have been made for me by the B. K. Elliott Company, of Pittsburgh. They are largely handmade, and the average wholesale price is about $10 a pair.

A SIMPLE AND INEXPENSIVE CHIN REST FOR USE WITH A TANGENT SCREEN

LOUIS C. RAVIN, M.D., TOLEDO, OHIO

In taking central fields with a Bjerrum screen it has seemed desirable to use a chin rest. This not only makes the patient more comfortable but insures better fixation of the central fixation target.

The use of an ophthalmic instrument table with a clamped-on chin rest, such as can be purchased from a manufacturer of optical instruments, has proved to be satisfactory. It was my desire, however, to make a less bulky and less expensive chin rest for use in the office. Practically any floor lamp stand with a thumbscrew adjustment, as illustrated here, may be used. The flexible tubing with the lighting fixture is removed. The movable tubular shaft may be replaced with an iron bar, as I have done, or it may be used as it is. The chin rest piece [1] is then attached to the rod shaft by grinding the shaft down at one end to fit into the opening in the chin rest. The small screw in



Chin rest for use with the tangent screen.

the chin rest piece is tightened, thus fixing it to the rod. If a solid iron rod is not easily obtained, a small piece of solid metal rod may be fitted into the tubular shaft and held in position with a small bolt or rivet. The end of this solid bar is then ground to fit into the chin rest piece. If one does not have the inclination or the facilities to do this bit of metal handiwork, any metal workshop can do this at a reasonable price.

The stand fits easily into a small space, is simple to use and is inexpensive.

316 Michigan Street.

1. Purchased from Bausch & Lomb Optical Co.

Ophthalmologic Reviews

EDITED BY DR. FRANCIS HEED ADLER

SOME BASIC PRINCIPLES OF DARK ADAPTATION

ROBB McDONALD, M.D.*
PHILADELPHIA

The physiology of rod and cone vision has been under investigation for many years, and many significant contributions have been made within the past few years, notably by Hecht and his associates in this country and Lythgoe and his associates in Great Britain. These studies, combined with the increasing knowledge of the biophysics of the eye and the chemistry of the vitamins, enable one to approach the problem of dark adaptation and its clinical significance without the skepticism manifest a few years ago. The greater part of this investigative work has been published in journals not always accessible to ophthalmologists, and frequently an advanced knowledge of physics and chemistry is necessary to interpret the findings. In this paper an attempt is made to review the problem in a brief and simplified manner and to give the present status of dark adaptation and the chemical basis of vision.

Schultze [1] in 1866 was the first to suggest that the retina possesses two types of receptor cells, but it was not until 1895 that the duplicity theory was finally established by von Kries.[2] In brief, it proposed that the cones are concerned chiefly with visual acuity and color discrimination at high intensities of illumination, while the rods are responsible for vision at low intensities of illumination, at which time the vision is most effective in the periphery of the retina and is colorless. Parsons introduced the terms photoptic for vision at high intensities of illumination and scotoptic for vision at low intensities of illumination. Therefore, photoptic vision is essentially cone vision and is chromatic, and scotoptic is essentially rod vision and is achromatic.

* Research Fellow in Ophthalmology.
From the Department of Ophthalmology, the University of Pennsylvania.
This work was supported by a grant from the John and Mary Markle Foundation.

1. Schultze, M.: Zur Anatomie und Physiologie der Retina, Arch. f. mikr. Anat. **2**:175, 1866.

2. von Kries, J.: Ueber die Funktion der Netzhautstäbchen, Ztschr. f. Psychol. u. Physiol. d. Sinnesorg. **9**:81, 1895.

The effect of abrupt changes from light to darkness is to lower the visual acuity; this phenomenon is well known. Coincident with the lowering of visual acuity, there is an increase in the light sensibility of the peripheral portion of the retina. This quantitative increase in the retinal sensitivity is known as dark adaptation. Dark adaptation is measured by determining the minimum intensity of a small area of light which is just perceptible to the eye at different time intervals after exclusion of all other light. This minimum intensity which is just perceptible is called the threshold. Hecht has emphasized that the factors to be considered in any determination of dark adaptation are: (1) the intensity and duration of the preadapting light and (2) the area and wavelength of the testing light, the duration of its exposure, the region of the retina stimulated, the size of the pupil and the exact intensity of the test light at any time during the course of dark adaptation.

Aubert [3] in 1865 was the first to describe the increased sensitivity of the eye when it is kept in the dark. During the latter part of the nineteenth century other investigators, notably König and Ritter [4] and Abney and Festing,[5] were concerned chiefly with the wavelength and the threshold of light just necessary to be visible in the dark-adapted eye. This work has been repeated several times since then, the most accurate determinations being those of Hecht and Williams [6] and of Kohlrausch.[7] They took into consideration the energy distribution of the spectrum (which the earlier workers did also, but they were handicapped by lack of modern apparatus) and found that the maximum visibility at low intensities was reached with light of a wavelength of 510 millimicrons. The same procedure has been used to determine the maximum visibility at high intensities, but here it was found by measuring the relative energy at different wavelengths required to match a high constant brightness. The maximum visibility was shown to be at 555 millimicrons, which is nearer the red end of the spectrum; this shift is the well

3. Aubert, H.: Physiologie der Netzhaut, Breslau, E. Morganstern, 1865.

4. König, A., and Ritter, R.: Ueber den Helligkeitswerthe der Spektralfarben bei verschiedener absoluter Intensität, in Festschrift zur Feier des siebzigsten-Geburtstages von Hermann von Helmholtz, Leipzig, L. Voss, 1891, p. 309.

5. Abney, W. de W., and Festing, E. R.: Color Photometry, Proc. Roy. Soc. London **50**:371, 1891.

6. Hecht, S., and Williams, R. E.: The Visibility of Monochromatic Radiation and the Absorption Spectrum of Visual Purple, J. Gen. Physiol. **5**:1 (Sept.) 1922.

7. Kohlrausch, A.: Untersuchungen mit farbigen Schwellenprüflichtern über den Dunkeladaptationsverlauf des normalen Auges, Arch. f. d. ges. Physiol. **196**: 113. 1922.

known Purkinje phenomenon. Chart 1 shows the relation between the wavelength and the relative energy required to produce a specific brightness at high and at low intensities.

This shows the well known phenomenon that the light-adapted and dark-adapted eyes have nearly the same threshold for red light. In other words, the color-colorless or photochromatic interval is longest for the short waves, i. e., violet and blue, while the interval for red is very small, i. e., "red crosses the threshold colored." The importance of this phenomenon is apparent. If the test flashes are made with a red light of 680 millimicrons, the results will record practically cone

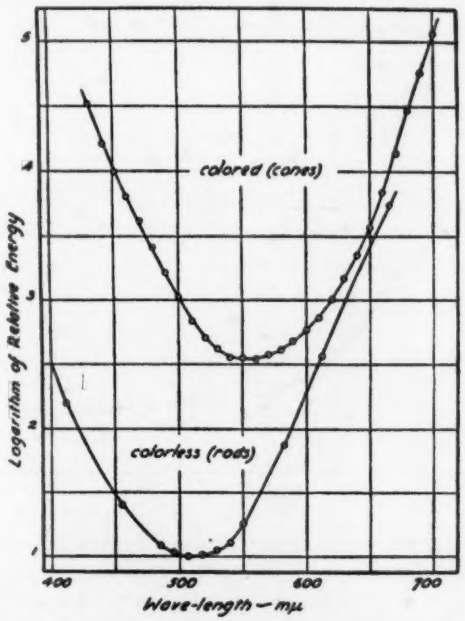


Chart 1.—Relation between the wavelength and the relative energy required to produce a specific visual effect at high and low illuminations. (From Hecht, S.: Rods, Cones, and the Chemical Basis of Vision, Physiol. Rev. **17**:242, 1937.)

behavior only. When blue light is used, one will obtain the maximum function of the rods (chart 2). If one reduces the intensity of a light by reducing the amount of current, the color of the light will change, especially at an extremely low intensity. Hence it is important that the intensity of the test light be reduced by filters of a neutral tint rather than by reducing the current by means of a rheostat.

The earlier workers did not recognize the factor of cone adaptation, the principal reason being that it takes place rapidly, and they plotted their results on a linear scale as sensitivity of the retina, which method

of plotting obscured their findings. Hecht has recalculated Piper's [8] data, which show, along with the work done by him and his co-workers,[9] that the cones do adapt themselves. Hecht's measurements of cone adaptation were made with red light and also with small 2 degree fields centrally located, both of which show the character and the course of cone adaptation.

The importance of adequate fixation and of knowing what portion of the retina is being stimulated by the test flash is shown in chart 3. With the eye completely dark adapted, the threshold for a 2 degree retinal field was determined at the fovea and at various points in the nasal and temporal portions of the retina. This shows clearly that the more peripheral the test flash the lower the threshold, owing to the increasing predominance of rods in the peripheral portion of the retina.

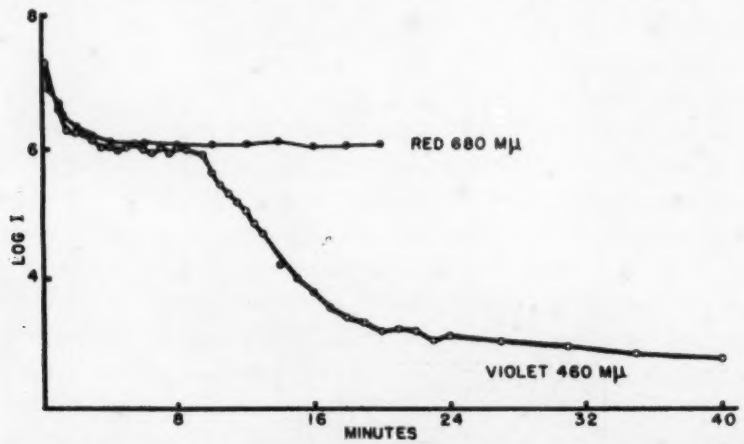


Chart 2.—Course of dark adaptation following light adaptation to 4,900 millilamberts. The solid circles represent the course as measured with red light of 680 millimicrons; the open circles, as measured with violet light of 460 millimicrons.

The control of the retinal location of the test flash by adequate fixation is one important feature which is absent in most of the popular instruments now used in clinical work. Sloan [10] recently reviewed the technics

8. Piper, H.: Ueber Dunkeladaptation, Ztschr. f. Psychol. u. Physiol. d. Sinnesorg. **31**:161, 1903.

9. Hecht, S.: The Nature of Foveal Dark Adaptation, J. Gen. Physiol. **4**:113 (Nov.) 1921. Hecht, S.; Haig, C., and Chase, A. M.: The Influence of Light Adaptation on Subsequent Dark Adaptation of the Eye, ibid. **20**:831 (July) 1937. Hecht, S.; Haig, C., and Wald, G.: Dark Adaptation of Retinal Fields of Different Size and Location, ibid. **19**:321 (Nov.) 1935.

10. Sloan, L. L.: Instruments and Technique for the Clinical Testing of Light Sense: III. Control Fixation in the Dark-Adapted Eye, Arch. Ophth. **22**:228 (Aug.) 1939.

for the clinical testing of the light sense and emphasized the importance of maintaining fixation. The subjective difficulties of this alone are apparent.

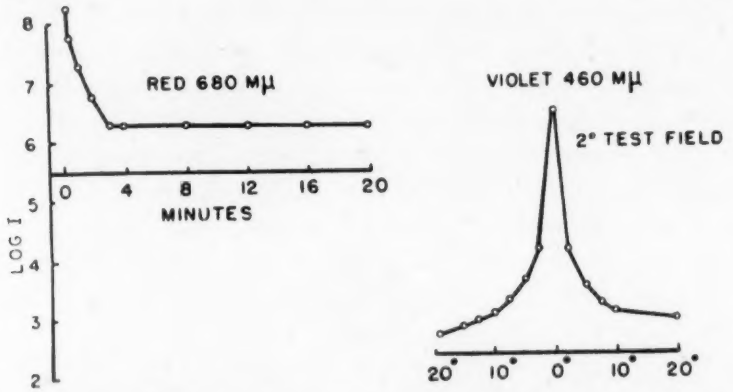


Chart 3.—The left part of the chart represents the course of dark adaptation as measured with red light. With the eye completely dark adapted and using a violet filter in the test beam, the threshold (right side of the chart) was determined at the fovea and at various points up to 20 degrees on either side of the fovea.

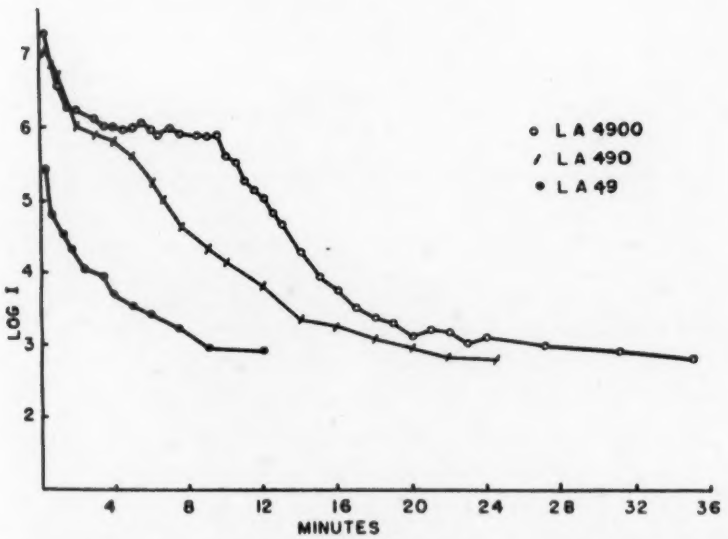


Chart 4.—Course of dark adaptation following various intensities of light adaptation. (The numbers in the right hand corner represent the intensity in millilamberts.)

Dark adaptation presupposes light adaptation. By increasing the intensity or time of the preadapting light, the recovery is naturally delayed. Chart 4 shows this clearly. The higher the intensity of the

preadapting light, the higher the initial threshold and the more prominent the cone adaptation. The rod-cone transition time is also delayed. The initial rod adaptation is masked in the cone adaptation.

Chart 5 shows the course of dark adaptation in a normal person as demonstrated with the Hecht apparatus. Haig, Hecht and Patek [11] expressed the belief that it is important to be able to show both rod and cone adaptation adequately in the same curve. The first part of the curve represents the adaptation of the cones, and the plateau is known as the cone plateau. The time of the sudden break in the curve is known as the rod-cone transition time, while the lower curve represents the adaptation of the rods and the lower plateau is called the final rod threshold. It is this threshold that most of the popular instruments

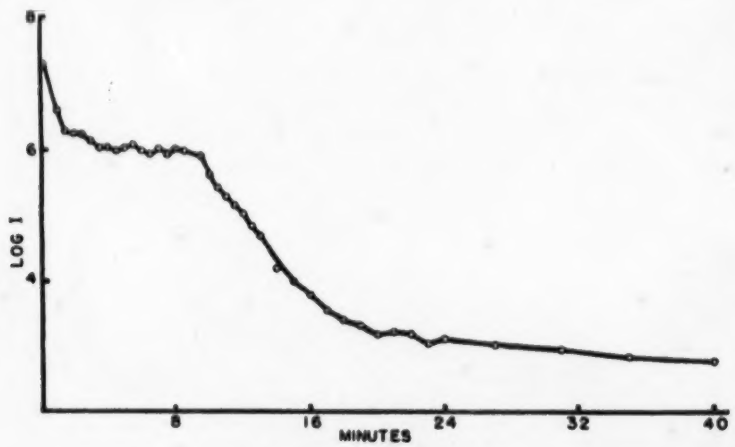


Chart 5.—Course of dark adaptation in a normal person following light adaptation at 4,900 millilamberts. The test flash subtended a retinal field 3 degrees in diameter and 7.5 degrees to the nasal side of the fovea. The test was made with a violet filter in the beam, and the test light was exposed for one-fifth second.

are concerned in measuring and that is the most reproducible in the clinical determination of dark adaptation, though its value is dubious unless the retinal location of the test flash is adequately maintained.

The remaining factors that must be considered are the area and duration of exposure of the testing light and the area of the pupil. For short exposures and small areas, the product of the intensity and the exposure time are constant (Graham and Margaria [12]). In most

11. Haig, C.; Hecht, S., and Patek, A. J.: Vitamin A and Rod-Cone Adaptation in Cirrhosis of the Liver, Science **87**:534 (June 10) 1938.

12. Graham, C. H., and Margaria, R.: Area and the Intensity-Time Relation in the Peripheral Retina, Am. J. Physiol. **113**:299 (Oct.) 1935.

instruments now in use an area exactly large enough to give a uniform cross section of the retina is exposed just long enough to be within the physiologic limits of the retinal action time. The size of the pupil is usually taken into account for accurate investigations, as the physiologic properties of the retina are concerned with apparent brightness rather than external brightness. The apparent brightness is expressed as external brightness in millilamberts times $10/\pi$ times pupil area in square millimeters, the unit being a photon. The use of an artificial pupil, the fixation of the pupil with miotics and photographing the pupil and computing its area have all been utilized. However, the pupil changes in size so rapidly from light to dark adaptation that except in precise work it need not be taken into account, though if the pupil is miotic and fixed, as in Argyll Robertson pupils, the threshold will be generally raised as the retinal illumination is reduced.

Thus any instrument for the clinical determination of dark adaptation should take into account the intensity and duration of the preadapting light and the area, color, retinal location and duration of the testing light. These can all be made constant, the only variable being an adequate range of intensity of the test light. The intensity should be plotted on a logarithmic scale against time in minutes as the abscissa. The use of a logarithmic plot is necessary because of the tremendous increase in sensitivity of the retina, an increase which may be on the order of 100,000/1. Plotted on a linear scale, the true course of dark adaptation is masked.

With the discovery of visual purple by Boll [13] in 1876 and its extraction from the retina by Kuehne [14] in 1879, it was natural to associate it with the visual process. In fact, Parinaud [15] in 1881 associated night blindness with deficiency in visual purple. The earlier workers, however, were chiefly concerned with the absorption spectrum of visual purple. If visual purple is the photosensitive substance responsible for rod vision, then the primary law of photochemistry should be fulfilled; that is, that only that light which is absorbed can initiate a chemical change. The absorption spectrum of visual purple and the spectral sensitivity of the eye at low intensities are closely related—a fact which one would expect to find if visual purple is responsible for the chemical initiation of the visual response. This relation is demonstrated in

13. Boll, F.: Zur Anatomie und Physiologie der Retina, Monatsber. d. berl. Akad., Nov. 12, 1876, p. 783.

14. Kuehne, W.: Chemische Vorgänge in der Netzhaut, in Hermann, L.: Handbuch der Physiologie, Leipzig, F. C. W. Vogel, 1879, vol. 3, p. 235.

15. Parinaud, H.: L'héméralopie et les fonctions du pourpre visuel, Compt. rend. Acad. d. sc. **93**:286, 1881.

chart 2 of an article by Ludvigh.[16] The minimum energy required to produce a bleaching effect on visual purple has also been determined and closely follows the curve for the absorption spectrum. Thus the close correlation between the minimum energy required to produce the sensation of light, the absorption spectrum and rate of bleaching of visual purple all point to it being the photosensitive substance in the rods responsible for the increased sensitivity in dark adaptation. Wald[17] recently isolated a photosensitive substance in the cones which he has called iodopsin and which is chemically distinct from visual purple.

Kuehne, in his classic monograph, described the bleaching of visual purple when acted on by light and its recovery when kept in the dark. Practically all his original observations have been confirmed, and a great deal has been added to the knowledge of the chemistry of visual purple within the past few years. It is generally accepted that visual purple is a conjugated carotenoid protein; its molecular weight is about 800,000 as determined by the diffusion method (Hecht, Chase and Shlaer[18]), though Lythgoe and Goodeve[19] found it to be nearer 100,000 with the ultra centrifuge. It has also been determined that visual purple may regenerate in two ways, directly from its photoproducts or from newly supplied material. The discovery by Fridericia and Holm[20] and of Tansley[21] that the rate of regeneration of visual purple in animals on a vitamin A–deficient diet was reduced and the experiments of Yudkin, Kriss and Smith[22] in relieving vitamin A deficiency by feeding whole retina proved rather conclusively that vitamin A must in some way be concerned with the visual response. Confirmation of this was definitely established by Wald[23] when he isolated vitamin A from the

16. Ludvigh, E.: Determination and Significance of the Scotopic Retinal Visibility Curve, Arch. Ophth. **20**:713 (Nov.) 1938.

17. Wald, G.: Photo-Habile Pigments of the Chicken Retina, Nature, London **140**:545 (Sept. 25) 1937.

18. Hecht, S.; Chase, A. M., and Shlaer, S.: The Diffusion Coefficient and Molecular Size of Visual Purple, Science **85**:567 (June 11) 1937.

19. Lythgoe, R. J., and Goodeve, C. F.: Visual Purple, Tr. Ophth. Soc. U. Kingdom **57**:88, 1937.

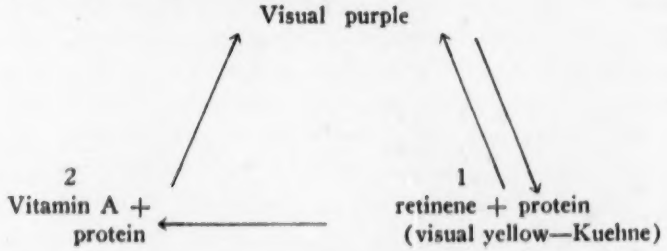
20. Fridericia, L. S., and Holm, E.: Experimental Contribution to the Study of the Relation Between Night Blindness and Malnutrition: Influence of Deficiency of Fat-Soluble A Vitamin in the Diet on the Visual Purple in the Eyes of Rats, Am. J. Physiol. **73**:63 (June) 1925.

21. Tansley, K.: The Regeneration of Visual Purple: Its Relation to Dark Adaptation and Night Blindness, J. Physiol. **71**:442 (April) 1931.

22. Yudkin, A. M.; Kriss, M., and Smith, A. H.: Vitamin A Potency of Retinal Tissue, Am. J. Physiol. **97**:611 (July) 1931.

23. Wald, G.: Vitamin A in Eye Tissues, J. Gen. Physiol. **18**:905 (July) 1935; On the Distribution of Vitamins A_1 and A_2, ibid. **22**:391 (Jan.) 1939.

retina itself. Wald has suggested the following scheme to illustrate the chemical basis of the visual response:



When light acts on visual purple in the isolated retina or in solution, it is bleached by a photochemical process to visual, or indicator, yellow; this yellow product finally fades out entirely if the light continues, the retinene being converted into vitamin A plus protein, which product was originally called visual white. If the retina at 0 C. is exposed to light, visual yellow is formed but will not be decomposed to its colorless product, nor will it regenerate to form visual purple. However, at 25 C. visual purple can regenerate from retinene, and retinene can fade out entirely to its colorless product. This proves that the initial bleaching of visual purple to retinene is photochemical but that its recovery from retinene or the complete fading of retinene is a thermal process. Vitamin A is found only in small quantities in completely dark-adapted and bleached retinas; its greatest concentration is found in the colorless decomposition product of retinene, which one would expect from the schematic cycle proposed by Wald. The expression of the visual cycle in the form of this equation concedes, of course, that in constant light adaptation a steady state is reached in which the resynthesis of visual purple is of the same proportion as its bleaching by light.

The regeneration of visual purple in solution from its colorless product, as well as its delayed regeneration in cases of vitamin A deficiency, is the most conclusive proof that vitamin A is a precursor of visual purple as well as a product of decomposition. Wald and Clark [24] have shown in subjective experiments that the rate of regeneration of visual purple depends on the intensity and time of the preadapting light. If the preadapting light is of low intensity and acts for a short time, the recovery of visual purple is limited to reaction 1 in the visual cycle and is rapid; however, if the pereadapting light is of fairly high intensity and acts for a longer period, the recovery follows reaction 2; that is, the recovery of visual purple is more rapid from retinene than from vitamin A + protein.

24. Wald, G., and Clark, A. B.: Visual Adaptation and Chemistry of the Rods, J. Gen. Physiol. **21**:93 (Sept.) 1937.

Within the past few years the clinical application of dark adaptation as a test for vitamin A deficiency has been widely accepted. Bitot [25] in 1863 was probably the first to recognize that xerosis and the conjunctival lesions which bear his name were often related to night blindness. The relief of night blindness by the ingestion of fish livers has been known since the time of the Egyptians. Hecht and Mandelbaum [26] and Wald, Jeghers and Arminio [27] in well controlled experiments were able to show conclusively that experimental vitamin A deficiency caused a rise in the visual threshold during dark adaptation. Chart 6 shows the characteristic change in the dark adaptation curve in vitamin A deficiency. The fact that the cone as well as the rod threshold is raised would imply that vitamin A is also concerned in the visual cycle of the photopigments of the cone. Haig, Hecht and Patek [11] have

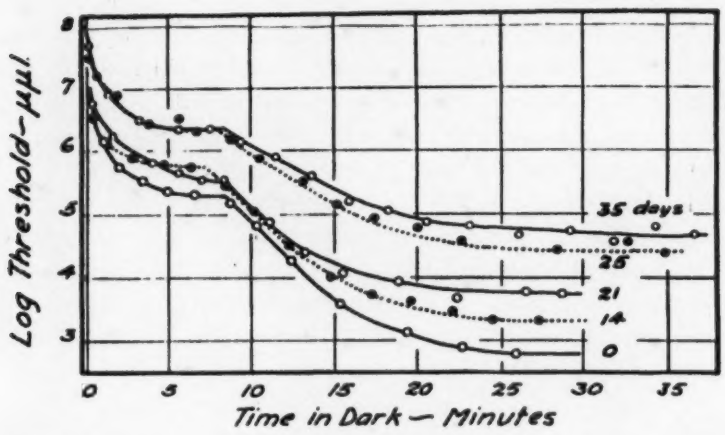


Fig. 6.—Change in the course of human dark adaptation in experimental vitamin A deficiency. (From Hecht, S., and Mandelbaum, J.: The Relation between Vitamin A and Dark Adaptation, J. A. M. A. **112**:1910 [May 13] 1939.)

also shown that in cirrhosis of the liver the rod-cone transition time is delayed, a fact which differentiates it from experimentally induced vitamin A deficiency and serves to emphasize that it may be important to obtain the entire adaptation curve with well defined cone adaptation.

The literature abounds with reports of dark adaptation as a test of vitamin A deficiency. Many suggestions have been devised to

25. Bitot: Mémoire sur une lésion conjunctivale non encore décrite, coïncidant avec l'héméralopie, Gaz. hebd. de méd. et de chir. **10**:284 (May) 1863.

26. Hecht, S., and Mandelbaum, J.: (*a*) Rod-Cone Dark Adaptation and Vitamin A, Science **88**:219 (Sept. 2) 1938; (*b*) The Relation Between Vitamin A and Dark Adaptation, J. A. M. A. **112**:1910 (May 13) 1939.

27. Wald, G.; Jeghers, H., and Arminio, J.: An Experiment in Human Dietary Night-Blindness, Am. J. Physiol. **123**:732 (Sept.) 1938.

simplify and hasten the procedure. It must be remembered, however, that dark adaptation is a physiologic phenomenon that requires time and that there are probably other factors concerned with dark adaptation besides the regeneration of visual purple. Apart from the subjective difficulties of the test, the exact metabolism of vitamin A in the body or the individual daily requirements are not yet known for certain.

Theories do not always fit the facts, and the value of dark adaptation as a routine test of vitamin A deficiency can be established only by a critical analysis of the results obtained. Unfortunately, in one's enthusiasm the basic physiology is sometimes neglected, and a true appreciation of the significant changes is missed.

News and Notes

GENERAL

The following item is taken from a recent number of the *British Medical Journal:*

Prevention of Blindness.—"A great piece of work in the spread of the knowledge of the causes of blindness and the means of preventing this catastrophe was done by the former Prevention of Blindness Committee of the Union of Counties Association of the Blind. When that committee was dissolved the work was taken over by a special committee of the Ministry of Health, which is continuing the analysis of the certificates of blindness prepared for the local authorities throughout the country. There has been some feeling that a voluntary committee, as apart from a Government committee, might serve a useful purpose in driving home the lessons of these statistical returns to masters of industry and local authorities. Accordingly the National Institute for the Blind, which has done so much and such valuable work for the blind, has appointed a prevention of blindness sub-committee. Its personnel is representative of all classes, lay and medical. Its chairman is Dr. C. G. Kay Sharp of Leeds. He commented upon the work of the new committee in his address at the conference of the Wales and Monmouthshire Regional Council of the Blind in Colwyn Bay. The National Institute for the Blind has done another good piece of work in preparing a report on blindness in India (Blindness in India, London, National Institute for the Blind, 1939. London, W.1). In a foreword Sir Michael O'Dwyer says there is no country in the world to-day where the affliction of blindness is so widespread as in India, nor where the ratio of blindness to population (350 millions) is so high. The totally blind are estimated at one and a half millions, the partially blind at three millions. Again, there is no civilized country in which so little is being done by the State, by public bodies, by voluntary associations (which hardly exist in India), and by private philanthropy to prevent blindness or to alleviate the lot of the blind. Among the reasons for the failure to tackle the problem are primarily the fatalism, common in the East, of regarding physical affliction as an act of God; the strength of the family and caste system, which, though producing many admirable results, limits the outlook and prevents the growth of a civic sense; the fact that nine-tenths of the population live in small and scattered villages or hamlets remote from the amenities of civilized life; and that only one-tenth are able to read and write. The report of the National Institute for the Blind includes an appeal to the Government of India. The International Association for the Prevention of Blindness has issued another number of its journal, which is a model for international publications, for it prints its matter in parallel columns of French and English. This issue deals with the recent annual session in London, at which Dr. Park Lewis of the U.S.A. was awarded the gold medal of the association for his great work in America. There are

reports on ophthalmia neonatorum in various countries; of particular interest are the notes from Dublin showing the excellent effect of prophylaxis. There are papers on eye diseases in workers by C. Coutela, and on lighting in schools by N. Bishop Harman. Of great interest is a note by H. Schröder on a small village called Titepec in Mexico, where all the inhabitants, indigenous and strangers, become blind. Investigations suggest that this blindness is caused by mosquitos which infect the people with a blinding worm of the genus Onchocerca."

Summer Graduate Course.—The eighteenth annual summer graduate course in ophthalmology and otolaryngology will be given in Denver, July 29 to Aug. 10, 1940. The list of guest teachers for the course in ophthalmology will be: Dr. Ramon Castroviejo, New York; Dr. John Hargreaves, Randolph Field, Texas; Dr. Placidus J. Leinfelder, Iowa City; Dr. Isaac S. Tassman, Philadelphia; Dr. Theodore L. Perry, Boston, and Dr. Sydney Walker, Chicago. The guest teachers for the course in otolaryngology will be: Dr. C. C. Bunch, St. Louis; Dr. A. J. Cone, St. Louis; Dr. W. J. Mellinger, Santa Barbara, Calif.; Dr. Harris Peyton Mosher, Boston; Dr. Samuel Salinger, Chicago, and Dr. Thomas Gooch Tickle, New York.

The fee for both weeks is $50 and for one week only, $30. This includes the cost of attending round table luncheons.

Obituaries

WEBB WILLIAM WEEKS, M.D.
1886-1940

After a lingering illness, Webb Weeks died at his home in New Canaan, Conn., on Jan. 10, 1940—a grievous blow to his friends and patients as well as to the medical profession at large.

He was born in Corry, Pa., on Oct. 24, 1886, the son of Frank Elmer and Eliza Cook Weeks. After his preparatory years at Corry High School, he entered Columbia University, graduating with the degree of Bachelor of Arts in 1910 and the degree of Doctor of Medicine in 1912. He then served a two year surgical internship at the Presbyterian Hospital in New York. After this, he began his training in ophthalmology at the New York Eye and Ear Infirmary. On the completion of this internship, he became associated with his distinguished uncle, Dr. John E. Weeks, until he entered military service.

His experience in the army was wide and varied, for after a short training period at Fort Sill, Okla., he went to France. Here he did active ophthalmologic duty both in evacuation and in base hospitals, and for this service he received two promotions. On his return to this country he was assigned to Fort McHenry, Md., where he worked with Dr. John M. Wheeler, gaining a large experience in plastic surgery. He was honorably discharged in July 1919, with the rank of major.

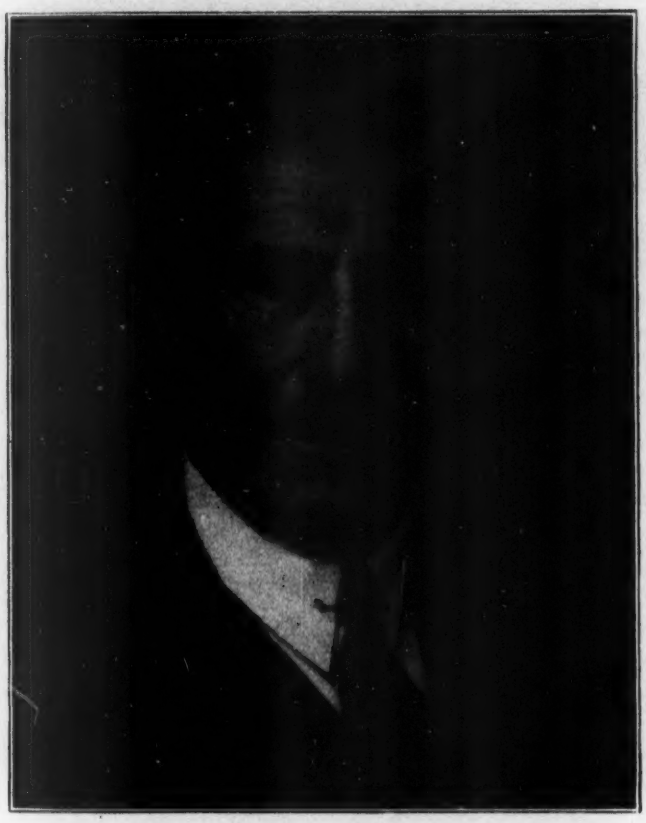
On resuming his work with Dr. John E. Weeks, his field of activity rapidly enlarged, and he soon became one of New York's leading ophthalmologists. His tireless energy, his keen clinical judgment and his surgical dexterity enabled him to profit to the fullest extent from this rare opportunity. A wise and experienced teacher had in him an apt and willing pupil.

He worked faithfully to the very last for the New York Eye and Ear Infirmary, serving it with true devotion and loyalty in almost every capacity. Starting as an assistant surgeon, he steadily earned promotions, until at the time of his death he was its executive surgeon. He was also director of the ophthalmic service of Bellevue Hospital and attending ophthalmologist to Beth Israel Hospital as well as consultant ophthalmologist to Rockefeller Institute, Norwalk (Conn.) General Hospital, Greenwich (Conn.) Hospital and Elizabeth A. Horton Hospital, Middletown, N. Y.

In addition to these clinical positions, he was professor of ophthalmology at New York University. His interest in undergraduate teach-

ing had been fostered by his predecessors, Dr. John E. Weeks and Dr. John M. Wheeler, under whom he had served as instructor and clinical professor before being appointed in 1928 to the professorship.

These responsibilities did not deter him from being a regular attendant at medical meetings. He served as chairman of the Eye, Ear, Nose and Throat Section of the New York State Medical Society in 1935 and of the Section of Ophthalmology of the New York Academy



WEBB WILLIAM WEEKS, M.D.
1886–1940

of Medicine in 1935 and 1936. He was president of the New York Ophthalmological Society in 1938. He took an active interest in the affairs of the American Academy of Ophthalmology and Otolaryngology, being a frequent lecturer at its instructional courses. His spirit of unselfishness was typically exemplified by this incident. Last October, in spite of great physical weakness and discomfort, he insisted on conducting one of these courses, doing it with his customary enthusiasm and thoroughness. He was also a member of the American Medical Associa-

tion, the American College of Surgeons, the American Ophthalmological Society and the Société française d'ophtalmologie.

He was not a prolific writer, but his articles were always cleancut, concise and practical. He was a contributor not only to the usual periodicals but also to Blumer's "Practitioner's Library of Medicine and Surgery" and to Berens' "The Eye and Its Diseases." He was actively interested in teaching operative surgery on the cadaver, giving much of his time and energy to this work. As an outgrowth of these courses, he prepared a manual on "Surgery of the Eye," in which he concisely portrayed the surgical procedures he had found useful.

He was a member of the University Club, the Country Club of New Canaan, the Wee Burn Club of Noroton, Conn., and the Phi Gamma Delta fraternity. He was also a member of the Quiz Medical Society and the Hospital Graduates Club, whose meetings he seldom missed.

In 1918 he married Ruth Thayer, of New Canaan, Conn., who with two children, John and Deborah, survives him. His home life was a happy one, for, although his professional activities demanded much of him, he always found time to hide away in New Canaan. A round of golf or a few sets of tennis were his chief diversions, with a detective story to top off a busy day.

In spite of all his accomplishments, a friend thinks first of him as a man, for to have known Webb was to have loved him. His genial nature, his generosity, his unselfishness and his high sense of integrity made him a delightful companion and a true friend. His boundless enthusiasm and great sense of fair play were ever present, both at work and at play. To those numbered among his friends his passing has left a void, never to be filled.

JOHN H. DUNNINGTON.

Obituaries

EUGEN VON HIPPEL
1867 - 1939

Eugen von Hippel, born in Königsberg, Germany, in 1867, was the son of Arthur von Hippel, professor of ophthalmology. So one might say that he was born with an aptitude for ophthalmology. But he was not only the son of a famous father. He acquired a place of honor among the ophthalmologists of the world by his own efforts. After being graduated from medical school, he had special training in internal medicine under Erb and in pathologic anatomy under Arnold. Then he turned to ophthalmology and became resident, assistant professor and associate professor in the ophthalmic hospital of the University of Heidelberg under the leadership of Theodor Leber. Thorough clinical training combined with scientific work was characteristic of this school. This principle remained with von Hippel all his life. One could fill many pages explaining all the work of Eugen von Hippel, but I want to emphasize only the most important of his scientific productions.

Scientifically, he was first of all a pathologist. Theodor Leber, Ernst Fuchs, Eugen von Hippel, Anton Elschnig and Joseph Meller are supposed to be the best ophthalmic pathologists in German-speaking countries. Eugen von Hippel himself always examined the rich material of enucleated globes in the ophthalmic hospitals in Heidelberg (1892 to 1909), Halle (1909 to 1914) and Göttingen (since 1914). In doing this, he not only illuminated the diagnosis of many cases but was stimulated to intensive research work on special topics. His work on siderosis bulbi (1893 to 1894), on glaucoma (1910) and on tuberculosis of the eyeball (1917 to 1918) are examples of profound anatomic and clinical studies. He never overestimated his own findings. When it appeared that his conception was wrong, he did not hesitate to admit it. For example, in the nineties he believed that tuberculosis, in addition to congenital syphilis, played a great role in the causation of keratitis parenchymatosa. He arrived at this opinion because of two observations: He had found epithelioid and giant cells on microscopic examinations in a case of keratitis parenchymatosa. He had also noted the presence of a disease of the joints, which was supposed to be tuberculous. When later in his own hospital, in the new era of syphilitic pathology, investigations made it evident that the foregoing criteria were

no proof of tuberculosis and that congenital syphilis was practically the only source of typical keratitis parenchymatosa, Eugen von Hippel did not hesitate to accept this idea.

Von Hippel not only was a pathologist but was occupied with experimental work. His investigations on the development of the normal eye and of malformations of the eye became the basis of all research in this field. He was the first who studied successfully the origin and inheritance of coloboma of the eye. He arrived at his conclusions by embryologic analysis of early stages, by experimental breeding and by the study of serial sections vertical to the fetal fissure (*Foetalspalt*). His three masterly monographs are on malformations of the eye.[1]

In these monographs as well as in his work on the diseases of the optic nerve and on the cornea and in his many other articles, three points are especially admirable: the clear and concise language, the separation of certain and uncertain facts and the critical attitude he had toward his own findings and toward those of other investigators.

The name of von Hippel will always be connected with the disease which he first presented as a "very rare disease of the retina" and later described histologically. This condition is now known throughout the whole world as Hippel's disease (or Hippel-Lindau's disease). His opinion that the principal feature of the disease is an angiomatous tumor formation in the retina was first doubted but is now recognized as correct.

Also, his view based on Cushing's work on the belief that the choked disk is a pure pressure phenomenon was finally accepted. In many articles and lectures he pointed out that the tumor-choked disk has to be treated operatively by decompression, with or without removal of the growth in the brain. He felt deeply the responsibility of recommending a dangerous operation on the brain of a patient with choked disk and normal or nearly normal vision, but he felt that this was the correct procedure.

Without mentioning all the other articles of von Hippel, it must be said that he was in the true sense of the word a good clinician, familiar with all regions of the eye; that he examined every patient with great accuracy and knowledge, and that he was a good surgeon and a highly honored chief.

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1. von Hippel, E., in von Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, ed. 2, Leipzig, Wilhelm Engelmann, 1901. von Hippel, E., in Schwalbe, E.: Die Morphologie der Missbildungen des Menschen und der Tiere, Jena, Gustav Fischer, 1909. von Hippel, E.: Missbildungen, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1928, vol. 11, pt. 2.

A few more words about the man. It is a great satisfaction for me, after having collaborated so many years with von Hippel, to speak of this often misunderstood teacher and friend.

Eugen von Hippel was by birthplace and nature an East Prussian. Duty was for him the superior law. An honest mind and reliability were to him indispensable. He seemed often to be cold and unapproachable. but this was only the expression of a certain kind of shyness and lack of flexibility. He had few friends, but very close ones; his best friend and companion, who took life so seriously, was his charming wife. More than most persons knew, he loved gaiety, humor, nature and music. It was a real pleasure to see this earnest man laughing so hard that the tears ran down his face or to observe him playing with his grandchildren. In those moments his longing for warmth and sunshine became obvious.

An outstanding side of his character was his feeling for justice and objectivity; because of this, he was a highly esteemed member of the faculty. His many pupils knew that they always had in him, in any emergency, a just advisor. On the other hand, he never was inclined to be a politician and to foster relations to procure favors for himself or for his pupils.

All in all, he was a real gentleman, a good ophthalmic surgeon, a successful investigator, a fine chief and a faithful friend.

It is a pity that because of sickness he was not able, after having resigned in 1934, to work out his plans and to give to his colleagues the results of his many unpublished studies.

JOSEPH IGERSHEIMER.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Biochemistry

THE OXIDASES AND REDUCTASES OF THE LENS. H. VON EULER, H. HELLSTROEM, F. SCHLENK and G. GUENTHER, Arch. f. Ophth. **140:** 116 (Feb.) 1939.

Cattle and rat lenses were examined and found to contain all enzymes necessary for glycolysis, whereas some of the most important oxydases, like cytochrom, were missing. The well known presence of large amounts of ascorbic acid and of sulfhydryl compounds (glutathione) in the lens was confirmed. P. C. KRONFELD.

Conjunctiva

BITOT'S SPOTS IN CEYLON. L. NICHOLLS and A. NIMALASURIYA, Lancet **1:** 1432 (June 24) 1939.

Nicholls and Nimalasuriya encountered a condition in the bulbar conjunctiva of several hundred malnourished children and other persons in Ceylon, which they refer to as Bitot's spots. The pathologic changes, as seen by them, are of a definite type but do not conform to some of the descriptions given by other observers. They have never seen Bitot's spots extending to the cornea, for they do not regard the changes in the cornea which occur in keratomalacia as extensions of Bitot's spots; and the spots in the great majority of their cases have in no way resembled foam. Bitot stated that all his patients had night blindness, but this has not been present in most of the authors' patients. Bitot's spots tend to be chronic, and it is necessary to give large doses of fish liver oils or concentrated preparations of vitamin A to clear them. The authors state that there may be two forms of xerosis, or keratinization, of the bulbar conjunctiva, an acute form in which the changes take place rapidly, forming loose accumulations of degenerative epithelium, which appear foamy, and a chronic form in which the accumulations of epithelium take place more slowly and are more compact. If this is so, possibly the first form is more likely to occur as a rare condition in countries in which diets deficient in vitamin A are not in common use, and the second form, as in the authors' patients, will be seen in countries in which the inhabitants have become more or less biologically adapted to diets deficient in this vitamin and consequently their reactions to the deficiency are more chronic. J. A. M. A.

CONJUNCTIVITIS CAUSED BY A FOREIGN WOOD, MAKORÉ: REPORT OF A CASE. DEFRANCE, Bull. Soc. d'opht. de Paris **51:** 90 (Feb.) 1939.

A cabinetmaker had gotten some sawdust in his right eye, which caused redness and rhinorrhea with tearing for some two weeks. On

the second occasion the sawdust caused a persistent irritation, redness and lacrimation for two or three weeks. After a third attack examination showed normal lids, but the bulbar conjunctiva was markedly vascularized. The cornea was entirely normal, as were the iris and lens. The ocular tension was 18. There was no adenopathy. A smear of the bulbar conjunctiva showed an absence of organisms. Zinc sulfate, used locally, did not help the condition. Experimentation with wood powder in a rabbit's eye produced a marked reaction. Defrance concludes that makoré is more irritating than ordinary wood powder. Makoré wood was found to be impregnated with zinc, copper and mercury in fine powder form. It is felt that these metals account for the reaction. Whether the mechanism is entirely one of mechanical irritation or sensitivity could not be decided.

L. L. MAYER.

Comparative Ophthalmology

THE EYE OF ARGYROPELECUS HEMIGYMNUS. F. CONTINO, Arch. f. Ophth. **140:** 390 (April) 1939.

Argyropelecus hemigymnus ("half-naked silver hatchet") is a small deep-sea fish which is found in the Straits of Messina. The author has studied about 100 specimens, representing all stages of development. The adult fish is from 3 to 4 cm. long and possesses so-called telescopic eyes, that is, eyes of approximately cylindric shape. The retina is situated at the base of the cylinder. The cornea contributes the lateral portion of the wall and the convex top of the cylinder. Only the latter is used for seeing. These eyes are inserted vertically in the head of the adult fish, so that most of the animal's field of vision lies above its head. The punctum remotum is situated 20 mm. above the eyes. The lens is spherical and protrudes markedly into the anterior chamber. The action of the retractor lentis has a negative accommodative effect and moves the punctum remotum to a point about 1 meter from the eyes. The retina contains only rods. The cornea is apparently impermeable to ultraviolet rays. The animal's eye is well equipped for the perception of the low intensities of light which prevail in the deeper strata of the sea.

P. C. KRONFELD.

Cornea and Sclera

RECURRENCE OF SYPHILITIC INTERSTITIAL KERATITIS. E. DALSGAARD-NIELSEN, Acta ophth. **17:** 38, 1939.

The incidence of recurrence of attacks of interstitial keratitis has been variously reported at from 5 to 17 per cent. The author is convinced that many of these recurrences are spurious; that is, they do not represent a real recurrence of keratitis but rather a recurrence of iridocyclitis, or a reengorgement of the deep corneal blood vessels as a result of irritation.

A reexamination of 173 patients who had formerly had interstitial keratitis failed to reveal any instance of true recurrence.

O. P. PERKINS.

BLUE SCLERA. H. L. JENSEN and K. K. ORTMANN, Ugesk. f. læger **101:** 275 (March) 1939.

Jensen and Ortmann, reporting 2 cases of Lobstein-Eddow's disease, osteopsathyrosis idiopathica, state that in the disorder blue scleras, a tendency to fractures and otosclerosis constitute a triad. As seen in their second case, blue scleras are not always accompanied by the tendency to fractures. There is generally a proportionality between the degree of coloring and this tendency. All authors agree that blue scleras are the dominating symptom. The color has been observed in 5 generations and established in 50 descendants of 1 person. A certain intensity of the coloring, a familial character and the combination of osseous and auditive stigmas in at least 1 member of the family are necessary for a positive diagnosis. The abnormal fragility of the bones depends on insufficient periosteal ossification coincidentally with inability of the bone tissue to take up calcium. The patients may become greatly deformed; in cases of extreme involvement they are referred to as "men of glass." The more underlying cause of the symptom complex is unknown. While in 1 family the disorder has appeared only in 20 male members, as a rule both men and women are affected. Transmission is probably dominant. The disorder may skip several generations, to reappear as the result of exogenic (disease) or endogenic factors (puberty or gravidity).

J. A. M. A.

Experimental Pathology

ARTIFICIAL ACHROMATOPSIA PRODUCED BY DAZZLING. Y. LEGRAND and E. GEBLEWICZ, Bull. Soc. d'opht. de Paris **51:** 171 (March) 1939.

It has been well known for a long time that color vision is less stable in lateral than in foveal vision. Apparently the saturation of a light impinging on the periphery of the retina decreases with time. That effect becomes considerably more marked if the light, instead of being continuous, is interrupted at a frequency of from forty to fifty per second. Experimenting with monocular vision, the authors have investigated a region 15 degrees from the fovea. If a dazzling light is used, the recognition of colors is reduced to a minimum. The implication theorized is the absence of cones and predomination of rods. One may think that the phenomenon of synchronization may so affect the nerve as to permit only uncolored stimuli to reach the cortex. The authors believe that the explanation is still unfounded but that the phenomenon proves that in all cases the lateral portion of the retina possesses special properties at high levels of brilliancy.

L. L. MAYER.

ACTION OF MINERAL DUSTS ON CONNECTIVE TISSUE, AS STUDIED WITH THE CORNEAL MICROSCOPE. A. POLICARD and J. ROLLET, Compt. rend. Soc. de biol. **130:** 954, 1939.

Traces of sterilized mineral dusts were inserted by a minute oblique incision in rabbit corneas which had been anesthetized with cocaine

hydrochloride. Coal dust incited no reaction, the carbon particles remaining at all times sharply delineated. Quartz and other silicas (opal, sand and fullers earth) produced a mild, slowly developing interstitial reaction, evident by the twelfth day as a whitish halo, consisting of cellular infiltration. With mica and sericite, the reaction was slight and transient. Permutite and cobalt arsenate, however, occasioned an early and severe reaction consisting of a grayish halo about the deposit and edema of the stroma and overlying epithelium.

J. E. LEBENSOHN.

General Diseases

DYSOSTOSIS CRANIO-FACIALIS (CROUZON). A. C. KRAUSE and D. N. BUCHANAN, Am. J. Ophth. **22**: 140 (Feb.) 1939.

Krause and Buchanan discuss malformations of the head, their classification and the symptoms, signs, prognosis and treatment of craniofacial dysostosis. They report a case in a 2½ year American boy and give the following summary:

"Reported in this article is a case of dysostosis cranio-facialis or Crouzon's disease with typical symptoms and confirmed by roentgen-ray examination. There is no apparent record of this disease in the American literature. In spite of operative decompression of the cranium and right orbit there is no reason to believe the prognosis will be favorable for either the eye, mentality, or life."

W. S. REESE.

General Pathology

THE ERYTHROCYTE–PLASM CHLORIDE RATIO IN OCULAR DISEASES. D. MICHAIL and P. VANCEA, Compt. rend. Soc. de biol. **130**: 1043, 1939.

A definite hypochloremia, indicative of a tendency to alkalosis, is found in glaucoma, detachment of the retina, optic neuritis, atrophy of the optic nerve, opacities of the vitreous and phlyctenulosis; an increased chloride ratio is noted in interstitial keratitis, sympathetic ophthalmia and disciform keratitis.

J. E. LEBENSOHN.

Lids

A CASE OF ALEUKAEMIC LYMPHOSIS INVOLVING THE UPPER LIDS, WITH PATHOLOGICAL FINDINGS. F. TOOKE, Brit. J. Ophth. **23**: 444 (July) 1939.

A man aged 65 was admitted to the hospital with a pendulous right lid. A tumor was presented. The skin of the lid was not discolored and was movable over the underlying tumor. The palpebral conjunctiva was thick and lusterless and a pinkish gray, resembling somewhat sodden blotting paper. The upper lid of the left eye presented prac-

tically the same features. Except for a moderate degree of chemosis about the accessory lacrimal glands, the globes appeared normal. There was a uniform adenopathy. Roentgenograms showed marked enlargement and increased density involving the roots of both lungs. This may have been due to hypertrophied glands. Biopsy of the tumors and of the posterior cervical glands gave a picture corresponding to that found on the borderline between lymphatic leukemia and a relatively mature form of lymphosarcomatosis. The author is inclined to classify the disease among the rather immature forms of lymphatic leukemia. The blood picture showed evidence of marked anemia, with a tendency for the cells to be somewhat larger than normal and to have poor regenerative ability. The white blood cells showed deficiency in the number of the myeloid elements, with some immature forms. The lymphocytes were increased; the increase appeared to be due to the presence of immature lymphoblastic cells, corresponding to those to be met with in the lymph glands.

The concluding paragraph of the article contains the following statements:

"This case, therefore, is one of a systemic lymphoid proliferation, which apparently from the progressive changes in the blood picture has involved the bone marrow, spleen, and lymph glands of the patient, as well as in an unusual manner, the eyelids. The proliferation is of a comparatively active form, and falls in its intensity and character between that met with in lymphatic leukaemia and that in lymphosarcomatosis. For this reason it is best classified as a leukaemic form of lymphosis, with unusual involvement of the eyelids and with an activity of cell proliferation bordering on the lymphosarcomatoses." W. ZENTMAYER.

Methods of Examination

A COMPARISON OF LENS AND SKIASCOPE METHODS IN RETINOSCOPY WITH UNDILATED PUPILS. W. J. B. RIDDELL, Brit. J. Ophth. 23: 387 (June) 1939.

The author gives the following summary of his article:

"A useful type of skiascope has been re-described.

"It has been used for hospital refraction work for over thirty years, and has proved a valuable time saving device.

"Figures provided by two hundred and fifty cases in which both trial frame and skiascope were used have been compared.

"A high degree of correlation was found.

"It is suggested that this devise might be employed in the construction of refraction curves from unselected samples of the population.

"The skiascope readings tended to be lower (i. e. more myopic) than the lens methods." W. ZENTMAYER.

ANALYSIS OF THE JUDGMENT OF RELATIVE POSITION: PRELIMINARY COMMUNICATION. P. C. LIVINGSTON, Brit. J. Ophth. **23:** 540 (Aug.) 1939.

The object of this paper is to bring into the foreground certain features of binocular vision which do not appear to have received full recognition and which, studied more fully, appear to have a close association with depth perception. Considered here, the term "depth perception" means the highest stratum of spatial recognition. A rotating depth perception apparatus is described. The test is based on the three pins of Helmholtz. The observer, at a distance of 11 feet (3 meters) from the pins, is asked to reset, by means of a cord, the middle pin in a position which he feels will make all three pins equidistant from him. Four perimeter positions are employed. It is believed by this procedure that the two visual characters are assessed, namely: (1) the sensitivity of the retinas to stimulation at disparate points, and (2) the psychovisual response to such stimuli, which calls for interpretation varying in acuteness according to the rotated position of the pins.

A second apparatus, consisting of a rotating stereogram and pictures, is used.

Experiments with these charts have revealed already that the majority of observers experience alternate vision and that there are marked variations in the quality alternation. W. ZENTMAYER.

Neurology

PAPILLITIS AND PAPILLEDEMA IN MULTIPLE SCLEROSIS. S. SUGAR, Am. J. Ophth. **22:** 135 (Feb.) 1939.

Sugar comments on the polymorphic manifestations of multiple sclerosis and the paucity of cases showing papillitis and papilledema. He gives the following summary:

"Two cases of choked disc occurring in multiple sclerosis are presented together with a review of the literature.

"In any case of choked disc with marked impairment of vision multiple sclerosis should be considered in the differential diagnosis.

"Recognition of the occurrence of this condition may help avoid unnecessary neurosurgical procedure." W. S. REESE.

GLIOMAS OF THE PONS. B. J. ALPERS and J. C. YASKIN, Arch. Neurol. & Psychiat. **41:** 435 (March) 1939.

Most pontile gliomas occur in children. Of the 11 tumors in this series, 8 occurred in children under 11 years of age. In most of the cases the illness began with diplopia and headache. The most striking of all the signs of pontile glioma were the paralyses of the cranial nerves, which were present always in greater or lesser degree. The abducens nerve was most frequently affected. R. IRVINE.

A Sign of Facial Palsy. R. Wartenberg, Arch. Neurol. & Psychiat. **41:** 586 (March) 1939.

Decrease of vibration in the upper lid felt by the examiner's palpating finger, which exerts upward pressure on the upper eyelid as the patient closes the eye, constitutes the finest and most reliable sign of facial palsy.

R. Irvine.

Foville's Syndrome: Record of a Case. J. R. Mutch, Brit. J. Ophth. **23:** 225 (April) 1939.

A man, aged 56, complained of failing vision and watering of the left eye. The positive symptoms were: paralysis and wasting of all the muscles of the left side of the face; left internal strabismus; loss of conjugate movement of each eye to the left; ptosis on the right; unequal pupils; horizontal nystagmus when the patient looked to the right; slurring of speech; sclerosis of the retinal vessels, and unsteadiness of gait with a tendency to fall to the left.

Mutch gives an exhaustive analysis of the symptoms, a description of the anatomy of the pons and its blood supply and a discussion of the relation of the symptoms to the nuclei. On the basis of the evidence supplied, the sudden onset, the nonprogressive nature of the lesion, the state of the retinal arteries and the fact that the lesion is confined to such a small area of the pons, the author made a diagnosis of thrombosis of a median branch of the basilar artery.

The article is illustrated.

W. Zentmayer.

Ocular Muscles

Congenital Abducens Paralysis. C. Apple, Am. J. Ophth. **22:** 169 (Feb.) 1939.

Apple reviews paralysis of the abducens nerve as to cause, preponderance on the left side and important objective findings, namely, restriction of abduction, restriction of adduction, retraction, oblique upward and downward movements, protraction, convergence insufficiency and torsion movements. He reports 3 cases from a total of 15 that were observed at the ophthalmic clinic of the University of Illinois College of Medicine in the past ten years. The patients in these 3 cases were personally observed and operated on to determine the underlying anatomic condition and to correct the strabismus.

W. S. Reese.

Parasites

Myiasis Due to Oestrus ovis. Temple, Harant and Viallefont, Arch. Soc. d. sc. méd. et biol. de Montpellier **20:** 26 (Feb.) 1939.

Oestrus ovis habitually lays its eggs in the eyes and nostrils of sheep, goats and dogs and only rarely in the human eye. Two cases of myiasis due to Oestrus ovis are reported in human beings. In 1 case a soldier complained of having something in his left eye since the previous evening. With the slit lamp one could just discern the movements of an

almost transparent body. Only the darker hooks of the larva and the particles in the digestive tract were perceptible. With the aid of the slit lamp the larva was removed without difficulty with the patient under local anesthesia and was examined under the microscope. It was 1.5 mm. in length and 0.4 mm. in width. In the second case the patient, a man, felt that an insect had entered his left eye the evening before. Examination revealed six larvae. Clinical manifestations are limited to tingling and a slight conjunctival reaction. J. E. LEBENSOHN.

Pharmacology

THE EFFECT OF THE MELANOPHORIC HORMONE IN NORMAL PERSONS AND IN THOSE WITH RETINITIS PIGMENTOSA. G. BASILE, Ann. di ottal. e clin. ocul. **67**: 412 (June) 1939.

The author investigated the effect on light sense and dark adaptation of an extract of the intermediary lobe of the pituitary which was known to produce expansion of the melanophores in the skin and retina of frogs. The literature, in part conflicting, is discussed. One cubic centimeter of the solution employed contained 20 to 25 units, as determined by Jores. During light adaptation of ten minutes, several drops of the solution was instilled in the right eye of the subject, the left being used as the control. The light sense was tested with the adaptometer of Engelking after dark adaptation every five minutes until the end of a forty-five minute period. Twenty normal subjects were first employed. A definite acceleration in dark adaptation with an increase in the luminous threshold was observed in the eyes receiving the hormone.

A similar technic was carried out in 6 patients with retinitis pigmentosa showing marked night blindness. In all of these cases a definite rise in the luminous threshold and an increase in light sense were observed. In a third series, 7 patients with retinitis pigmentosa were given the hormone by subcutaneous injection, adaptation being tested before and during treatment. Injections of 0.5 to 1 cc. were given every two to four days and from three to nine injections. Marked increase in the light sense was observed after treatment in 5 of these patients, the vision and fields showing, on the contrary, no improvement. The response in 2 cases was less satisfactory, both of these cases showing a marked degree of night blindness. Further investigations are proposed to determine whether prolonged use of the hormone will affect the course of the disease. The mode of action on the retinal elements has not been determined. S. R. GIFFORD.

THE INFLUENCE OF RETROBULBAR INJECTIONS ON THE TENSION OF THE EYE. N. MEDVEDIEV and L. SATZ, Vestnik oftal. **14**: 102, 1939.

The authors gave retrobulbar injections of procaine hydrochloride and epinephrine hydrochloride in a solution of a 0.5 per cent to 18 rabbits and 29 patients with various diseases. There was a decrease in tension in the majority of the animals and patients, but in 6 patients an increase of the tension was observed after the injections, particularly

in the eyes with increased tension. Medvediev therefore thinks that retrobulbar injections should be given cautiously in cases of primary and secondary glaucoma. The increase of tension might be due to the needle and also to the mechanical pressure of the liquid.

O. SITCHEVSKA.

The Pupil

TONIC PUPILS AND ABSENT TENDON REFLEXES (ADIE'S SYNDROME). A. VEASEY SR., Northwest Med. **38:** 204 (June) 1939.

Veasey reviews the literature of Adie's syndrome and reports 2 cases of his own. The patient in the first case was an unmarried girl aged 18. She complained of the pupil of the right eye being larger than that of the left eye. A photograph showed that the condition was present at 9 years of age. Vision was 6/5 in each eye. The media and fundus were normal. The behavior of the pupils was typical of the syndrome. The pupils responded promptly to mydriatics and miotics. There was no Romberg sign; both knee jerks and elbow jerks were normal, but both ankle jerks were absent. The laboratory tests and physical examination otherwise gave negative results.

The patient in the second case was an unmarried woman aged 24. The pupil of the left eye had been dilated at least six months. The history was irrelevant. Examination revealed nothing of importance. The pupillary reactions were those of the syndrome. The pupils reacted to miotics and mydriatics. The visual acuity was normal. The media and fundus were normal. The knee, elbow and ankle jerks were absent on both sides.

W. ZENTMAYER.

Physiology

THE INFLUENCE OF CENTRAL NERVOUS SYSTEM ON THE PIGMENT MIGRATION IN THE RETINA OF THE FROG. H. M. BURIAN, Am. J. Ophth. **22:** 16 (Jan.) 1939.

Burian gives the following summary of his investigations:

"Experiments with strychnine and naphthalene have shown that the retinal pigment of dark-adapted frogs shows light position when the animals are poisoned with strychnine, and that in light-adapted frogs poisoned with naphthalene the retinal pigment assumes dark position.

"From this the author concludes that there is a regulating influence of the central nervous system on the position of the retinal pigment.

"In frogs, in which the optic nerve on one side was severed, the drugs did not influence the eye operated upon. The author concludes that the pathway through which the central nervous system exerts its influence must be located in the optic nerves, supporting Engelmann's theory of the existence of centrifugal, retinomotor fibers in the optic nerve.

"The position of retinal pigment appears to be influenced by the following factors: (1) the basic tonus of the central nervous system; (2) the 'light tonus' of the central nervous system; and (3) local humoral conditions due to the influence of light and various general metabolic factors."

W. S. REESE.

Retina and Optic Nerve

PATHOGENESIS OF THROMBOSIS OF THE CENTRAL RETINAL VEIN AND OF CONSECUTIVE GLAUCOMA. P. WEINSTEIN, Brit. J. Ophth. **23:** 396 (June) 1939.

Weinstein found that glaucoma developed in 23 of 50 persons with thrombosis of the central vein of the retina. The author gives the following summary:

"Thrombosis of the central retinal vein occurs in individuals of advanced age, whose blood-pressure is high (180 mm. of mercury or above), the amplitude of their tonoscillograms exceeding 15 mm.

"The histological examination of the central retinal vein discloses its walls to have thickened, its endothelium displaying hyaline degeneration and proliferation, the adventitia disclosing hyperplasia of connective tissue.

"In such cases thrombosis of the central retinal vein is followed by glaucoma, its main branch being obliterated.

"Glaucoma forms in such cases by accumulation of pathological products of altered metabolism (carbonic acid, lactic acid, acetic acid, citric acid, etc.), the vitreous body swelling gradually by their influence. Under the normal physiological conditions, hydration corresponds to 98.5 mm. of water, and under the influence of lactic acid augments to 166.0 mm.

"X-ray irradiative treatment of hemorrhagic glaucoma is indicated."

W. ZENTMAYER.

THE DISEASE OF LAURENCE-MOON-BARDET-BIEDL (RETINITIS PIGMENTOSA, POLYDACTYLISM, ADIPOSOGENITAL DYSTROPHY AND INTELLECTUAL DEFICIENCY). C.-I. URECHIA, P. VANCEA and L. DRAGOMIR, Ann. d'ocul. **176:** 274 (April) 1939.

This rare and interesting malady was reported by Laurence and Moon for the first time in 1866 in 4 sisters, in whom there was found retinitis pigmentosa associated with retarded physical and intellectual development. Bardet, in an excellent thesis in 1920, entitled "The Syndrome of Infantile Obesity with Polydactylism and Retinitis Pigmentosa," described the condition and drew attention to the fact that the malady seemed to still remain unknown. Two years later, in 1922, Biedl took up the study of the disease and added to the syndrome mental deficiency. He pointed out that in 2 of his cases there were present posterior cortical cataract and anal atresia. To date there have been about 150 cases reported.

The case is reported of a youth aged 21 whose father suffered from mental debility but was without any malformation. The case described is a classic one of the disease, which up to the present has been seen only in white persons.

There are five illustrations and five pages of bibliography.

S. H. MCKEE.

COAT'S RETINITIS. V. SPADAVECCHIA, Ann. di ottal. e clin. ocul. **67:** 321 (May) 1939.

The author reports a case of bilateral retinitis haemorrhagica externa occurring in a man of 40. The visual disturbance had begun one and

one-half years before he was seen by the author. Vision was reduced to 2/10 in the right eye and to perception of hand movements in the left eye. The fundus changes are well illustrated and showed the typical formation of connective tissue in the retina with dense bands connecting various retinal areas, many containing newly formed vessels. These were especially marked in the left eye, in which the disk was completely covered. The veins were large and tortuous, and the small branches were surrounded by tissue resembling glia. In both eyes a large subretinal mass was seen occupying a large part of the fundus and accounting for 9 diopters of hyperopia in the right eye and 20 diopters in the left, as determined by retinoscopic examination. General examination showed numerous telangiectases of the skin, moderate hypertension and slight enlargement of the liver and spleen. Microscopic study of the capillaries showed a moderate loss of tone in the venous branches of the capillaries. Tuberculin tests gave slightly positive reactions. The signs indicated a tendency to generalized venous stasis. The author believes that this abnormal condition of the veins may be of causative importance in relation to the ocular changes. The literature is discussed.

S. R. GIFFORD.

TREATMENT OF RETINITIS PIGMENTOSA WITH INTRAMUSCULAR INJECTIONS OF COD LIVER OIL. V. FILATOV and E. VERBITZKAYA, Vestnik oftal. **14:** 21, 1939.

Six patients suffering from retinitis pigmentosa were treated with intramuscular injections of pasteurized cod liver oil. In 3 patients the injections produced a marked and quick improvement of the function of the retina, disappearance of the night blindness and improvement of dark adaptation, visual fields and visual acuity. In 2 patients the treatment yielded moderate results, and in 1 there was no improvement. Though the period of observation is short (from one to four months), the authors think it worth while trying this treatment on a large number of patients.

Filatov believes that the action of the cod liver oil depends not only on vitamin A but on the products of disintegrated liver tissue. In order to verify this, two small pieces of conserved human liver were implanted under the skin of a patient with retinitis pigmentosa. The vision improved from 0.3 to 0.4, the visual fields increased about 10 degrees and the dark adaptation improved. The histories and visual fields of the patients are presented in the article.

O. SITCHEVSKA.

Trachoma

THE ÆTIOLOGY OF TRACHOMA. F. H. STEWART, Brit. J. Ophth. 23: 373 (June) 1939.

Stewart gives the following summary of his views concerning the etiology of trachoma:

"Trachoma is caused by the virus described in 1907, the most conspicuous form of which is the Prowazek-Halberstaedter inclusion body or P. K. A free extracellular stage also exists resembling in appearance

a polymorph bacterium. Inclusion bodies can be found in all cases of trachoma if examination is repeated. Allied diseases are paratrachoma (inclusion blennorrhoea and swimming bath conjunctivitis), psittacosis and granuloma inguinale, the parasites of which resemble that of trachoma. Reports on filtration through collodion membranes impermeable to bacteria, of 0.6 and 0.7μ a.p.d. are contradictory (1) that the filtrate is infective (2) that it is not so. The virus can be concentrated on the upper surface of such membranes. It has not been grown in any form of culture or on the chorio-allantoic membrane. Animals which can be infected with certainty in the conjunctiva are baboons and grivet monkeys. The virus can survive in the testicle of rabbits and guinea-pigs, and it is claimed will multiply in the intestines of a louse. The statement that trachoma is normally carried by lice needs confirmation. There is some experimental evidence that it is not carried biologically by lice or flies. Infection is spread by direct contact and may be carried mechanically by flies for a short time only, since the virus is killed by drying."

The article is illustrated.

W. ZENTMAYER.

Therapeutics

ACTION OF VITAMIN B_1 IN CERTAIN OCULAR DISEASES. G. CARLEVARO, Ann. di ottal. e clin. ocul. **67:** 355 (May) 1939.

The author has attempted to group a number of corneal conditions, including herpes zoster, herpes simplex, disciform keratitis, recurrent erosion and others, under the heading of neurotrophic corneal diseases. In a series of such cases crystalline vitamin B_1 was administered intravenously and ethylmorphine hydrochloride locally. In 6 cases of herpes simplex of the dendritic type, and in 1 of superficial punctate keratitis successful results were obtained. In another case of dendritic ulcer recurrences were noted in spite of treatment; there were also recurrences in a case of unusually severe diffuse keratitis. No result was obtained in a case of herpes zoster with iridocyclitis or in a case of disciform keratitis. In another case of disciform keratitis some improvement occurred under treatment. In only 1 case was there definite evidence of a vitamin-deficient diet, although a history of alcoholism, influenza and tuberculosis in several cases offered a possible explanation of a deficiency.

Vitamin B_1 was employed in a second series of cases of diseases of the optic nerve. In 3 cases of toxic amblyopia due to tobacco and alcohol good results were obtained, while no effect was noted in cases of retrobulbar neuritis due to multiple sclerosis and syphilis.

To determine the effect of vitamin B_1 on regeneration of nerve tissue, the author compressed the sciatic nerve of rabbits, treated alternate animals with vitamin B_1 and studied sections of the nerves after various intervals of one to sixty days. Some evidence was obtained indicating a more rapid repair of damage to the myelin sheaths in the animals receiving vitamin B_1. The literature is discussed, and a bibliography is included.

S. R. GIFFORD.

TREATMENT OF ACNE ROSACEA WITH EXTRACT OF THE CORTEX OF THE ADRENAL GLAND. R. THIEL, Klin. Monatsbl. f. Augenh. **102:** 394 (March) 1939.

An ointment containing zinc ichthammol has yielded good results in keratitis caused by acne rosacea but has failed in many cases, some of which were reported by Claussen and by Wilhelm. Thiel refers to contributing disorders in acne rosacea, such as subacidity, constipation, anemia and endocrine dysfunction, especially prior or during the menopause, and mentions Wadel's satisfactory experience in cases of acne rosacea with hormones of the hypophysis and of the cortex of the adrenal gland. Two cases of Thiel's own observation are reported in which acne rosacea of the face with recurring keratoconjunctivitis resisted various treatments. Both patients, a man aged 43 and a woman aged 51, recovered promptly after injections of an aqueous solution of extract of the cortex of the adrenal gland prepared after an especial method. The man received eight injections and the woman fifteen. Equally good results were obtained in 8 other patients. No untoward symptoms developed, except in 1 patient, in whom small abscesses formed at the site of the injection; they were attributed to local allergic reaction. The preparation is manufactured by the I. G. Farbenindustrie, A. G., Germany.

K. L. STOLL.

Toxic Amblyopia

INVERSION OF THE VISUAL FIELD FOR COLOR IN AMBLYOPIA DUE TO QUININE. C. DRACONTAIDIS, Ann. d'ocul. **176:** 437 (June) 1939.

In the foreign literature, especially in the Greek, many cases of quinine amblyopia are recorded in which there is noted a concentric shrinking of the limit of the visual field for plain and colored lights.

The writer has noted at the ophthalmological clinic at the University of Athens a considerable number of cases of amblyopia due to ingestion of quinine in which detailed examination of the color fields was made. In 8 of the cases of the previous year an inversion of the limit of the visual field for color was found. Examination showed a normal disposition of the limits of the visual fields for different colors, but a definite inversion of these was found. The 8 cases are described in considerable detail, with comments on each and the visual fields in each case. A bibliography accompanies the article.

S. H. McKEE.

Uvea

A NOTE ON CHRONIC IRIDO-CYCLITIS, WITH SPECIAL REFERENCE TO THE SARCOIDOSIS OF BOECK. R. KEMP, Brit. J. Ophth. **23:** 455 (July) 1939.

Kemp examined 25 patients with chronic iridocyclitis to establish to what extent such persons were actually suffering from generalized sarcoidosis. In all the cases the condition was chronic and untractable, and in none had the etiologic agent been found.

Based on this study, the author concludes:

"1. The incidence of non-specific chronic irido-cyclitis seems to fall into three age/sex groupings.

"2. Apart from this, present day clinical methods are unable to link the illness with any of the known aetiological causes. It may therefore be a disease *sui generis*.

"3. It follows a chronic progressive course, is not amenable to treatment and the visual prognosis is poor.

"4. Sarcoidosis is not a cause in the majority of instances."

W. ZENTMAYER.

CHOROIDITIS AREATA. K. SVEINSSON, Acta ophth. **17:** 73, 1939.

The author reports 4 cases of a fundus lesion which Professor Rønne has called choroiditis areata. The condition is thought to be the result of a congenital anomaly in the development of the pigment epithelial layer and of the choroid. It is bilateral, with a tendency to symmetry. A glistening white area of choroidal atrophy surrounds the disk, and similar tongue-shaped areas, with scalloped borders, radiate toward the periphery. The maculas are not involved, nor are there other pathologic symptoms or signs. Black and white drawings illustrate the 4 cases.

O. P. PERKINS.

Society Transactions

EDITED BY W. L. BENEDICT

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

DAVID WEBSTER, M.D., *Chairman*

ROBERT K. LAMBERT, M.D., *Secretary*

Dec. 18, 1939

Bilateral Subconjunctival Tumor. DR. ALBERT V. SARADARIAN.

Painless, extensive, subconjunctival salmon-colored tumors developed in the upper halves of both globes of McC., a white man aged 59, whose general health was good. He entered the Jersey City Medical Center Clinic and Hospital for observation and treatment. Examination revealed chronic sinusitis, severe caries, a faintly positive Mantoux test, an increased basal metabolic rate, right submental adenopathy, bilateral axillary and inguinal adenopathy, a shift to the left of juvenile non-segmented polymorphonuclear cells, mild secondary anemia and leukocytosis; biopsy showed numerous undifferentiated mast cells.

DISCUSSION

DR. JOSEPH IGERSHEIMER, Istanbul, Turkey: About fifteen years ago I encountered a case similar to the one reported by Dr. Saradarian. The patient was a woman of about 50 who was suffering from aleukemic leukemia.

Vaccinal Disciform Keratitis Following Accidental Inoculation of the Eyelid. DR. CHARLES A. PERERA.

This paper will be published in full, with discussion, in a later issue of the ARCHIVES.

Ocular Sensitivity to Nupercaine. DR. CHARLES A. PERERA.

This paper will be published in full, with discussion, in a later issue of the ARCHIVES.

Vitamin A and Vision. SELIG HECHT, PH.D., Columbia University.

Measurements of dark adaptation record the changing amount of light required for the threshold of vision during a stay in the dark subsequent to exposure of the eye to light. In general, the course of dark adaptation shows two portions. The first is an immediate and rapid decrease in threshold, which is associated with cone function; the second is a later and slower decrease in threshold, which is associated with rod function. These two parts of the course of dark adaptation may be demonstrated in a variety of ways, depending on the differences

between the rods and cones in their retinal distribution and in their sensibility to the spectrum.

The precise course of dark adaptation is influenced by several different factors: by the duration, intensity and color of the preadapting light and by the size, retinal location, color and duration of the test light used for measuring the threshold. In other words, the measurement of dark adaptation is not a haphazard process but must be made under rigidly defined conditions in order for the results to have precision and meaning.

Dark adaptation is an expression of the accumulation in the eye of photosensitive substances, such as visual purple in the rods and visual violet in the cones. This accumulation of sensitive materials is determined among other things by the vitamin A content of the diet, since night blindness due to dietary deficiency has been cured by the addition of vitamin A to an inadequate diet. In addition, vitamin A is formed in the retina when it is bleached. Thus there exists in the retina a chemical system in which vitamin A is both precursor and product of the principal photosensitive materials.

In terms of this chemical relation, efforts have been made to use measurements of the visual threshold as diagnostic signs for the vitamin A state of the body, particularly in cases of subclinical avitaminosis A. The results have been conflicting and have shown that enthusiasm is no substitute for adequate knowledge of dark adaptation and vision or for precise methods of measurement.

To establish critical information in this respect, an apparatus was designed which controls all the factors known to influence the progress and extent of dark adaptation. With this apparatus under standard fixed conditions, a survey was made of a reasonably large and normal group of persons in order to establish the norms for the various characteristics of dark adaptation. The most significant of these turned out to be the final threshold for cone vision, the final threshold for rod vision and the time for the point of transition from cone to rod function. Sex has no influence on any of these properties. Age increases the threshold both of the cones and the rods, though the cone-rod transition time is unaffected.

Experiments with 17 normal young men on controlled diets showed that most subjects respond immediately to a drastic reduction in the vitamin A content of their diet. There is considerable individual variation, but the rise in threshold is great and unmistakable and in most cases immediate. In 3 cases the rise was slight to begin with, and a rapid rise showed up only after two months of continued deficient diet.

Recovery from a deficient diet as measured by the visual threshold was nearly always slow. Ingestion of large single doses of vitamin A (100,000 to 500,000 U. S. P. units) produced variable reductions in the threshold, but the reductions were never large, and the dramatic results achieved by other workers have not been duplicated. The return to a normal diet supplemented by 20,000 or more units of vitamin A never produced a startling cure. The most rapid recovery of a normal threshold occurred in 2 subjects and required four weeks of an adequate diet. In most cases, however, the return of the visual threshold to normal took much longer and in some instances was not accomplished in three months.

Vitamin A is stored in the liver, and disturbances of the function of this organ may be expected to influence the visual threshold. Measurements of the dark adaptation of several patients with alcoholic cirrhosis of the liver showed changes resembling those of acute dietary avitaminosis A. These symptoms were removed by supplementing the patients' diets with large amounts of vitamin A.

The conclusion of all this is that measurements of dark adaptation when made under standard and precise conditions constitute a tool for discovering dietary deficiencies and disease conditions concerned with a deficiency of vitamin A.

The researches on which this lecture was based were made in collaboration with Drs. Joseph Mandelbaum, Charles Haig, Arthur J. Patek Jr. and Simon Shlaer. For specific references to the points briefly abstracted here, the reader is referred to a recent paper entitled "Relation Between Vitamin A and Dark Adaptation" (*J. A. M. A.* **112**: 1910-1916 [May 13] 1939).

Clinical Aspects of Vitamin A and Dark Adaptation. Dr. Francis Heed Adler, Philadelphia.

DISCUSSION ON PRESENTATIONS BY DRS. HECHT AND ADLER

Dr. Robb McDonald, Philadelphia: I feel that it is rather presumptuous of me to say anything after hearing these two presentations; my only excuse for doing so is that I have been using Dr. Hecht's apparatus for over a year and have been interested in studying the physiologic basis of dark adaptation. However, I should like to show two slides and to discuss some work I am doing with Dr. Adler in the department of ophthalmology at the University of Pennsylvania and how we hope to get to the basis of this problem.

The first slide depicts the electrical response in a single fiber of the optic nerve of a horseshoe crab, which goes to show that we are getting down to the basis of the visual response. This slide has nothing to do with dark adaptation but shows the effect of intensity of stimulation on the discharge. The spikes are action potentials, and the response varies with the intensity of illumination. The brighter the light, the shorter the latency and the greater the frequency of the response.

The next slide shows the change in the response to dark adaptation. Here again are demonstrated action potentials. There is a constant intensity of stimulus and a constant time of exposure. In the early responses after light adaptation there is a latency which is definitely longer than the latency shown after an hour, and the number and the frequency of impulses increase with dark adaptation. We have accumulated considerable data on this objective method, and I think that shortly we will be able to show that the character of the response in the dark-adapted state is not the same as in the light-adapted state. We also hope to clear up some other problems in the physiology of dark adaptation.

Dr. Benjamin Friedman: I should like to ask Dr. Hecht, first, whether during the course of the induced vitamin A deficiency his patients were able to distinguish the effects of this deficiency clinically, and, second, whether he has found any evidence to support the contention

that the brain is also a factor in dark adaptation or whether he feels that this is solely a peripheral phenomenon.

DR. SELIG HECHT: In answer to Dr. Friedman's first question, our subjects reported almost no subjective findings in their daily life. They were questioned regularly, and their fields were watched and their eyes examined; however, with the exception of 1 patient they reported nothing. This patient showed the most extreme response to the vitamin A deficiency. His threshold had increased nearly 2 logarithmic units. One day he said, "Last night I bumped into a wall which I should have seen but did not." That was the first report made of any subjective recognition that all was not normal. Since the threshold was 2 logarithmic units above normal, we became apprehensive and terminated the experiment, putting the subject on a normal diet, supplemented with vitamin A.

There has been a good deal of loose talk about vitamin A and night driving, and I may say from my own experience that it is largely unfounded. One of the subjects of these experiments, Dr. Mandelbaum, did a great deal of night driving and found no difficulty with it, undoubtedly because under ordinary circumstances the illumination that prevails is never near the threshold. Please remember what near the threshold means. It represents an extremely small amount of light, and I suppose if one were expected to function at this very margin of illumination, one would be sure to be affected and to notice an incapacity to see. But in the city and even in the country one is not subjected to that small amount of light.

Perhaps I may be pardoned if I tell the details of an experience with a colleague who was sensitive about his vision. He stated that he was certain he could tell merely by his night driving experience when he was getting an adequate amount of vitamin A and when he was not. His dark adaptation was measured when, according to his judgment, he was in fine condition, and a normal curve was obtained. I told him that the first time he felt he was in poor condition to come in for another test. He called up one day and said that he was in miserable shape. His dark adaptation was found to be precisely what it was before. The effect of vitamin A on night driving was reported by Jeghers in Boston. However, he used the biophotometer as the method of measuring the threshold, and this instrument used as he did is rather unreliable, to put it mildly. One cannot tell what it shows, because it is hard to say just what it measures.

The other point to which Dr. Friedman refers is probably the work of Elsberg, who insists that dark adaptation takes place in the brain. I am sure that Dr. McDonald's measurements which have just been shown demonstrate that it does not take place in the brain. These retinal potentials were taken from the isolated eye, freed from the brain; nevertheless they show adaptation of the same kind and order of magnitude as in the intact animal. Moreover, protozoa, clams, ascidians and even plants adapt themselves to darkness.

DR. WENDELL L. HUGHES: Have any measurements been made on the other eye when one eye is dark adapted? If so, I should like to know whether dark adaptation in one eye made any difference in the opposite eye. This remark is made with reference to Dr. Elsberg's work, reported here last year.

DR. SELIG HECHT: There has been a great deal of discussion as to whether the threshold with two eyes is the same as with one eye, and the problem is not settled. In this work the eyes can be measured alternately or simultaneously, and the result is practically the same. I could be more specific, since I know what Dr. Hughes is asking for, but I think I will let it go at that.

DR. E. M. JOSEPHSON: I should like to ask Dr. Hecht if the superfine dark adaptation test which he has used in his work is at all applicable clinically. Dr. Adler has shown that the dark adaptation may vary considerably in various areas in the retina. Clinically I have the feeling that it would be almost impossible to have a patient hold his eye so quiet for thirty minutes of testing or for one to get absolutely identical spots for repeated successive examinations. I have tried to do so, without much success. (The biophotometer, I have found, gives the clinically valuable data on the dark adaptation of the entire eye, in spite of its failure to yield ultrascientific data on the reactions of a single rod or cone.)

DR. FRANCIS HEED ADLER, Philadelphia: It is true that fixing is the bête noire of the whole problem, and I can say with confidence that the reason Dr. Hecht is so vehement about the biophotometer is that fixation is extremely poor with that instrument. With Dr. Hecht's instrument it is true the subject has to cooperate, but one does have more control of the fixation with that instrument than with any other I know of, and I agree that one can tell fairly accurately just what portion of the retina is being investigated.

DR. JOSEPH MANDELBAUM: The subject is not required to look at the fixing point and hold the fixation for thirty minutes. He is required to do so only during the minute or two that it takes to make a reading. In the interval, the subject can sit back and relax.

There was a point which Dr. Adler mentioned about corneal dystrophy. I have examined 3 patients with this condition. Instead of using the affected eye to record dark adaptation, I used the normal eye. Although there were no opacities which might account for it, I obtained deficient dark adaptation in 2 of these cases. I do not know whether vitamin A deficiency causes corneal dystrophy or not.

DR. JOSEPH IGERSHEIMER, Istanbul, Turkey: Behr has pointed out that the question of dark adaptation is important in the differential diagnosis between choked disk and optic neuritis. It would interest me to know whether Dr. Adler has had the same experience.

DR. FRANCIS HEED ADLER, Philadelphia: I have not, but I should take it for granted that the dark adaptation curve has the same value as the visual acuity test, which is one of the chief means of differentiating between neuritis and papilledema.

DR. FRANK D. CARROLL: With reference to Dr. Igersheimer's question, if a scotoma is present in the area tested, the dark adaptation curve is elevated. I have tested numerous persons with toxic amblyopia with the adaptometer devised by Dr. Hecht and have found in the area corresponding to the scotoma a definite elevation of the curve, whereas if another place on the retina is tested it may show no abnormality. As the toxic amblyopia gets better, the scotoma disappears and the curve for the area returns to normal.

DAVID H. WEBSTER, M.D., *Chairman*

ROBERT K. LAMBERT, M.D., *Secretary*

Jan. 15, 1940

Motion Picture Demonstration of Unusual Neuro-Ophthalmologic Conditions. DR. S. PHILIP GOODHART and DR. BENJAMIN BALSER.

DISCUSSION

DR. S. P. GOODHART: As Dr. Balser has stated, we are preparing an atlas for cinematographic demonstration of various forms of diseases of the nervous system. This atlas, describing the individual films for the instruction of students, will be made available to medical schools. The film presented here is one of this collection. In this film, as in our others, we present rather rare forms of ocular conditions with associated pathologic conditions of the central nervous system. All ophthalmologists are familiar with the intimate relation between the mechanism governing the function of the ocular structures and that governing the function of the central and peripheral nervous systems. Among the clinical syndromes presented here, that called "skew deviation" is one resulting from pathologic involvement of the brain stem; in the case presented it is of interest to note that a neoplasm of the posterior fossa caused pressure anteriorly and that the resulting ocular condition was relieved on removal of the neoplasm.

The study of three different forms of nystagmus is of clinical interest, as each form is shown as a part of a syndrome of extensive organic pathologic involvement and yet the result of a minute lesion, involving in each instance the posterior longitudinal fasciculus. The cases presented are of clinical as well as of anatomic interest and indicate the importance of evaluating a discrete pathologic process which makes its presence known by an easily overlooked clinical sign. Nystagmus, especially in cases of multiple sclerosis, usually affects both eyes.

The case of myasthenia gravis illustrated here is another example of the intimate association between ocular manifestations and more extensive disease within the nervous system. The patient came to the hospital complaining only of general weakness, and examination brought out occasional difficulty in fully raising the lids. Transitory muscular weakness and fatigue so characteristic of the disease were evident when the patient was asked to follow an object—the examiner's finger—as it moved rapidly in extreme lateral positions; one then observed a slowly increasing degree of ptosis with final closure of the eye due to the failing power of the levator muscles of the upper lids. With a few minutes of rest, power was recovered. The point is that only careful testing of the function of the ocular muscles gave the early objective findings of a serious neurologic condition.

The last condition demonstrated in the film, neuromyelitis optica, is a rare clinical entity. The clinical picture may show as its early manifestation beginning atrophy of the optic nerves, while the objective findings referable to the involvement of the spinal cord may be overlooked. This case again illustrates the close relation of the two branches

of medicine, ophthalmology and neurology, as demonstrated by some of the more unusual forms of neuropathologic involvement.

An Operation For Spastic Entropion. Dr. Raymond E. Meek.

This paper will be published in full, with discussion, in a later issue of the Archives.

Central Scotomas: Their Importance in Topical Diagnosis. Dr. Frank B. Walsh and Dr. Frank R. Ford.

This paper will be published in full, with discussion, in a later issue of the Archives.

A New Corneoscleral Suture. Dr. John M. McLean.

This paper was published in full in the March issue of the Archives, page 554.

DISCUSSION

Dr. Ramon Castroviejo: I should like to ask Dr. McLean three questions: In the series of 110 cases in which his sclerocorneal suture was used were there any instances in which either the suture or its scleral attachment was cut while making the incision? How many days after the operation is the patient allowed to get out of bed? How many days after the operation is the eye which is not operated on uncovered?

Dr. Benjamin Friedman: In tying the suture I noticed that there was a tendency for the lower lip of the wound to become everted. This is due to the difficulty in pulling the suture through the relatively thick cornea. I should like to ask whether reversing the direction of the suture would not tend to obviate this difficulty.

Dr. John M. McLean: Dr. Castroviejo asked if I ever cut the suture in making the section. Yes, I did that once. I do not think there is any excuse for it, but I did it. However, if I do cut the suture, I still have a prepared conjunctival flap, so if I care to I can use ordinary conjunctival sutures or, as I did in the case in which I cut the suture, I can rethread those tracks after Verhoeff's technic.

In regard to how many days after the operation I let the patient get up, that is variable. In that connection I might relate something about the first motion picture I showed. From the technical standpoint, it is not a good film. The patient was not cooperative. She was rolling her head all over the table, and I was following her, and the motion picture camera was following us both. She was a charming old lady from the Old People's Home and very, very senile. The night after her operation she became thoroughly confused and stood up in bed. Before the nurse in the ward could reach her she executed a practically perfect swan dive from the bed to the floor, striking the eye that had been operated on on the corner of the table. The intern had to use a half a dozen sutures to repair the laceration of her upper lid, but she did not burst the wound open, and her eye healed uneventfully. This incident represents one extreme in getting the patient up. I have had some old mountaineers from West Virginia who will not get up, but as a general rule I try to get the patients up as early as possible. I have never had any trouble attributable to getting them up too early when this

suture was used. In that respect I am held back a little because the general hospital routine is that which has gone on for many years. I should like to get these patients up as early as Dr. O'Brien does, the day after they are operated on or shortly thereafter, but that I have not been able to do routinely. The third question concerns the eye that is not operated on; the standard technic at the Wilmer Ophthalmological Institute, which has held over from the days when purely conjunctival flap sutures were used, is to leave both eyes bandaged for four days, and to unbandage the eye that is not operated on on the fourth day; however, if the patient becomes confused I unbandage this eye immediately in order to keep the patient in touch with reality as far as possible.

Dr. Friedman wants to know about reversing the suture and putting it in the other way around. I do not think it makes much difference. The needle is going to drag a little when it goes through the cornea. It drags a little when the Liégard or Verhoeff or any other technic is employed. I put the suture in this way because it was a little easier to see what I was doing. Is that what Dr. Friedman means?

DR. B. FRIEDMAN: No, I refer to the final stage when the suture is tied. One has to pull the suture through the corneal wound in a downward direction, which at the time the vitreous is exposed causes an undesirable gaping.

DR. JOHN M. MCLEAN: I do not do that ordinarily. When the operation is being photographed, in order to keep my hand from obscuring the view the hand is backward, and exactly the same thing is done in tying the suture at the end. I do tie it the way Dr. Friedman suggests unless I am trying to illustrate the procedure by motion pictures, and then I have to get my hand out of the way as far as possible. I have never had any trouble through loss of vitreous while tying sutures.

DR. JAMES W. SMITH: To what depth is the corneal slot fashioned with the Lundgard knife and what is the width of the suture material used in the flap?

DR. JOHN M. MCLEAN: The slot goes approximately halfway to the anterior chamber. For practical purposes it goes deep enough to get the needle through. The needle is known as Kalt's corneal needle. I cannot say just what is the size of the suture material, because it is sold under the name of Kalt's corneal silk, and I do not think the size is given.

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

ALEXANDER G. FEWELL, M.D., *Chairman*

WARREN S. REESE, M.D., *Clerk*

Dec. 21, 1939

Transcranial Extirpation of a Fibrohemangioma of the Orbit: Report of a Case. DR. BENJAMIN SOUDERS.

This article will appear in full in a later issue of the ARCHIVES.

The Extraocular Muscles in Myasthenia Gravis and Hyperthyroidism.
DR. MELVIN W. THORNER.

Palsy of the extraocular muscles is so commonly present in cases of myasthenia gravis that many patients with this condition are seen by the ophthalmologist first. The paralysis is characterized chiefly by the facts that it frequently changes from one muscle to another and that the weakness is greatly lessened by the administration of prostigmine. The current most generally accepted explanation of myasthenic weakness is that there is an area of deficient conduction of the nerve impulse at the myoneural junction. This (according to Dale) is partly dependent on the presence of acetylcholine at this junction. According to this hypothesis, acetylcholine is either destroyed too rapidly or is produced in insufficient quantity in the myasthenic patient. More recent work would indicate that the myoneural junction is not the sole site of the pathophysiologic disturbance in myasthenia gravis. The pathologic changes are not prominent. There are intramuscular collections of lymphocytes (the lymphorrhages), which are found most frequently in the extraocular muscles. Also, it should be noted that thymic abnormalities, chiefly neoplasms, are found at 50 per cent of autopsies.

In the case of hyperthyroidism a totally different situation exists. Approximately 50 per cent of patients with hyperthyroidism may present some degree of exophthalmos, although it may be necessary to use an ophthalmometer to detect the milder degrees. While the ultimate cause of exophthalmos is unknown, the proximate cause is hypertrophy of the orbital contents. In many cases this hypertrophy and mechanical distortion are so great that ocular movements are impeded. The explanations for exophthalmos that have been advanced are: 1. It is caused by excessive thyroid secretion. 2. It is caused by sympathetic stimulation of Müller's muscle. However, experimental evidence has shown that exophthalmos may be produced in thyroidectomized and sympathectomized animals by the administration of an anterior pituitary extract containing the thyrotropic hormone. The existence of true isolated extraocular palsies in hyperthyroidism is rare, occurring in 1 of 300 cases. The pathologic picture of hyperthyroidism consists of fairly constant lymphorrhages in the extraocular muscles and hypertrophy of the thymus gland; the latter change is not usually associated with the formation of a neoplasm.

The concomitant association of these two conditions in the same patient is an interesting phenomenon. When it occurs, as it rarely does, a type of "see-saw" balance is established between the two. When the hyperthyroidism is most marked, the myasthenic symptoms are least marked. It was possible in such a case (Relation of Myasthenia Gravis to Hyperthyroidism, *Arch. Int. Med.* **64**: 330 [Aug.] 1939) to establish a therapeutic balance for a time.

This presentation has been an attempt to show the difference in mechanism by which ocular movement is impaired in cases of myasthenia gravis and of hyperthyroidism. In addition, the mutual antagonism of the conditions, when they coexist, has been noted.

DISCUSSION

DR. I. S. TASSMAN: I should like to ask Dr. Thorner his explanation for the various muscles being affected at different times and for one

muscle recovering when another becomes affected, only to become again involved at a later stage.

It might also be of interest to know whether the effect of prostigmine in myasthenia gravis is produced by its action on the choline esterase, whereby it would serve to interfere with the esterase in its role as antagonist to the parasympathetic activity of acetylcholine.

DR. WARREN S. REESE: I should like to ask Dr. Thorner whether it is true that in these cases of myasthenia gravis the paralysis increases toward the end of the day.

DR. H. MAXWELL LANGDON: There is no doubt that patients with myasthenia gravis show more marked changes toward the end of the day than they do in the early morning. I have seen about 4 patients with this condition, and all of them showed less activity toward the end of the day not only in the ocular muscles but in other parts of the body.

The word "paralysis" in relation to these cases does not seem very accurate to me, although I suppose it is the best word available to describe the condition of the patients.

Myasthenia, suggesting a fatigue of muscles, is descriptive, and the condition does progress to actual loss of muscular function. Therefore, it seems to me that paralysis is not inexact but is rather inaccurate.

I was interested in the rather lengthy comparison of myasthenia gravis with hyperthyroidism. To me, the conditions are so different that if one has seen only a case or two of each there should be no difficulty in making a differential diagnosis.

DR. MELVIN W. THORNER: Dr. Tassman's question, as he probably suspected, is not easy to answer. In myasthenia, each muscle appears to have a certain limited rate of energy production. When this is used up, as for example in an external rectus muscle, it may no longer function until it has had a recovery period. During this recovery period, the internal rectus muscle may become exhausted and inactive. In this manner a plausible explanation for the rotation of weakness of the extraocular muscles may be built up.

While prostigmine is postulated either to inhibit the abnormally great destruction of acetylcholine (by cholinesterases) or to stimulate its production, neither of these two hypotheses is definitely proved. The blood esterase findings have not as yet shown sufficient agreement among investigators to afford a basis for a pedantic and categorical statement.

The aforementioned facts concerning the limited energy production in muscles might serve to explain why the myasthenic patient is weaker at night. The day's endeavors would be likely to have used up most of the available energy supply, so that at night the weakness is most marked. This clinical fact was noted by Erb and Goldflam and most of the clinicians following them, but this rule, as most others, has its exceptions. Some patients are worse in the morning than at night.

I agree with Dr. Langdon's abhorrence of the word "paralysis." Most generally, the term would broadly include any one of many conditions which have in common the inability to perform a movement voluntarily. The unsatisfactory word in such a definition is the word "voluntary," which could lead to a host of esoteric and philosophic arguments. All this is, of course, pointless when the mechanism underlying a "paralysis" is known.

A Clinical Evaluation of Dark Adaptation Tests. Dr. Francis H. Adler and Dr. Robb McDonald.

This paper will appear in full, with discussion, in a later issue of the Archives.

A Clinician's Experience with Sulfanilamide. Dr. Burton Chance.

The results of sulfanilamide therapy in a group of cases, including cases of trachoma, uveitis and exfoliative keratitis, is reported. Only small doses were taken by mouth, with remarkable effects. The almost miraculous alleviation of all symptoms which resulted should be ascribed solely to sulfanilamide.

Book Reviews

Hydrophthalmia or Congenital Glaucoma. Its Causes, Treatment and Outlook. By J. Ringland Anderson, M.C., M.D., B.S. (Melb.) F.R.C.S. (Edin.), F.R.A.C.S., D.O.M.S. (Lond.), Ophthalmic Surgeon to Alfred Hospital, Melbourne. With a foreword by Sir John Herbert Parsons, C.B.E., D.Sc., F.R.C.S., F.R.S. Price, 25 shillings net. Pp. 377, with 116 illustrations. Published for the British Journal of Ophthalmology, by the Cambridge University Press, London, 1939.

This monograph is one of the publications sponsored by the *British Journal of Ophthalmology*. It is a handsome volume, profusely and beautifully illustrated.

The subject of hydrophthalmia is exhaustively treated under the chapter headings of general etiology, differential diagnosis, the structure and development of the involved tissue, their embryology and comparative anatomy, the pathology of congenital glaucoma, pathogenesis, treatment, prognosis and general reflections.

The terms congenital glaucoma and hydrophthalmia are preferred by the author. He suggests that the use of all other terms be abandoned. The author states that "the condition to be described is that of an eye which has become enlarged under the influence of increased tension." Subsequently, he says that "the ocular condition that we are to consider is that which is due to a rise in tension occurring at so early an age that the coats of the globe distend." The latter definition seems to be more appropriate.

He considers that no hard and fast line divides the congenital, juvenile and adult forms of glaucoma. In the chapter on differential diagnosis, the condition of megalocornea is fully described.

In the study of the comparative anatomy of the parts involved, the author states that in the human eye the ciliioscleral sinus is generally so empty of uveal tissue that it appears like part of the angle. The disappearance of this meshwork gives the ciliary muscle maximum freedom but may be a real loss to the eye, if the supposition is right that a true pectinate ligament aids the circulation of aqueous by capillary attraction and by preventing the iris root from coming in contact with the cornea.

In 86 per cent of twenty-eight specimens of early hydrophthalmia, the cause of the condition was probably the fetal state or the abnormal development of the meshwork of the angle.

As to treatment of the local condition, in certain cases miotics appear to be beneficial and are therefore worthy of trial, but the author adds "the result is determined by the actual pathological state."

The author states that regarding operation one may say that any hope for success almost vanishes after the first year. The superiority of Elliot's operation is possibly masked by the fact that it is more or less in general use and therefore performed by more inexpert operators. Much can be hoped from the operation described by Barkan, for this

gives the surgeon a reasonable chance of establishing a channel of escape through the obstructing tissue at the angle by making an incision under direct and magnified vision.

The pocket attached to the inside of the backboard contains tables of pathologic observations in the author's cases and in those reported in the literature. A commendable feature is the summary or conclusions and the references at the end of each chapter. The subject matter is brought up to date. While the book is primarily a reference book, the chapter on treatment contains a critical consideration of all the different procedures, with an analysis of results.

The book will prove a valuable addition to the library of all students of ophthalmology.

WILLIAM ZENTMAYER.

Traité d'ophtalmologie. Published under the auspices of the Société française d'ophtalmologie, by P. Bailliart, C. Coutela, E. Redslob, E. Velter and R. Onfray, general secretary. Eight volumes, pp. 8,058, with 176 plates in color. Subscription unbound edition, 2,500 francs; bound edition, 2,800 francs. Single volume, 350 or 400 francs. Paris: Masson & Cie, 1939.

Volumes I and II were reviewed in the October 1939 issue of the ARCHIVES, page 713.

Volume III (1,146 pages, 460 figures, 9 plates in color) contains three subdivisions with the following titles: "Technic" (continued), "Visual Anomalies" and "Pathology."

In the part on technic of the laboratory the following subjects are considered: chemical and serologic examination of the blood, spinal fluid and intraocular fluid, by A. Dubois-Poulsen; bacteriology by L. Carrère; elements of pathologic technic by L. Carrère, and animal parasites of the eye, by G. Senevet.

Motility of the eyeball and binocular vision are then described under the following headings: "Examination of Motility of the Eyeball," by Jean Nordmann, and "Examination of Binocular Vision," by René Onfray.

The second main subdivision, "Visual Anomalies" is divided into chapters with the following titles: "Hypermetropia," Astigmatism" and "Anisometropia," by H. Joseph; "Myopia," by Jacques Mawas; "Presbyopia and Troubles of Accommodation," by L. Hambresin; "Vision and Correction of Aphakic Eyes," by Emile Haas; "Anomalies of Light Sense," by F. Bourdier, and "Anomalies of Color Sense," by A. Polack.

The principal subdivision in this volume is designated "Pathology" and is continued in volumes IV, V and VI. The subject is introduced by a consideration of general pathologic and biologic reactions with special application to the eye, which are considered under the following headings: "Pathology of the Cell" and "Inflammation" and "Tumors," by E. Redslob and L. Gery. This chapter of 174 pages is a most instructive presentation based on the point of view of general pathology. Chapters entitled "Ocular Allergy," by André Koutseff, and "Vitamins," by Nicholas Bezssonoff, are of great interest at the present day. Professor Terrien writes on the relation of general pathology to ophthalmology. A section entitled "Glands of Internal Secretion in Their Relation to

Ophthalmology" (100 pages) is from the pens of A. Franceschetti and G. Gorin. General ophthalmologic symptoms are reviewed by F. Terrien in a section which forms an introduction to the parts that follow, in which the diseases of each anatomic part are taken up in turn: diseases of the eyebrow, by H. Villard; diseases of the lids, by E. Aubaret; tumors of the lids, by Marcel Kalt; tumors of the caruncle, by Marcel Kalt, and disturbances of the motor apparatus of the eyelids, by Jean Sédan.

In volume IV (898 pages, 233 figures and 36 plates in colors) the general heading "Pathology" is continued, and the following conditions are taken up: lacrimal apparatus, by V. Valière-Vialeix; diseases of the conjunctiva, by G. Renard and Roger Nataf; trachoma, by A. Cuénod and Roger Nataf; conjunctival lesions occurring in general diseases or in diseases of the neighboring organs, lesions of the conjunctiva produced by certain chemical substances or by substances of animal or vegetable origin and conjunctival lesions produced by physical agents —light, radium, x-ray and electricity, by L. Genet; tumors of the conjunctiva, by Mérigot de Treigny; diseases of the cornea, by P. Prélat; other diseases of the cornea, by G. Kleefeld, and diseases of the sclerotic, by Paul-J. Petit.

The chapters on conjunctival diseases (G. Renard and Roger Nataf) and on trachoma (A. Cuénod and Roger Nataf) are outstanding, not only for the excellence of the scientific approach in the text but for the illustrations, many of which are in color.

ARNOLD KNAPP.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6°, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6°, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 33 Welbeck St., London, W., England.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. H. G. Ditroi, Szeged.
Assistant Secretary: Dr. Stephen de Grosz, University Eye Hospital, Maria ucca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

North of England Ophthalmological Society

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

Ophthalmological Society of Australia

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.
Place: Perth, Western Australia. Time: Sept. 2 and 7, 1940.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the Secretary, Dr. Mohammed Khalil.

Ophthalmological Society of the United Kingdom

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Oxford Ophthalmological Congress

Master: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.
Time: July 4-6, 1940.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

Polish Ophthalmological Society

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

Royal Society of Medicine, Section of Ophthalmology

President: Dr. Malcolm Hepburn, 111 Harley St., London, W. 1, England.
Secretary: Dr. C. Dee Shapland, 15 Devonshire Pl., London, W. 1, England.

Sociedade de Ophtalmologia e Oto-Rhino-Laryngologia da Bahia

President: Dr. Francisco Ferreira, Pitangueiras 15, Brotas, S. Salvador, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

Società Oftalmologica Italiana

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

Société Française d'Ophtalmologie

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

Society of Swedish Ophthalmologists

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 III tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Secretary: Dr. Derrick T. Vail Jr., 441 Vine St., Cincinnati.
Place: New York. Time: June 10-14, 1940.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Frank E. Brawley, 30 N. Michigan Ave., Chicago.
Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.
Place: Cleveland. Time: Oct. 6-11, 1940.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. Frederick Tooke, 1482 Mountain St., Montreal, Canada.
Secretary-Treasurer: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.
Place: Hot Springs, Va.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Secretary-Treasurer: Dr. C. S. O'Brien, University Hospital, Iowa City.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.
Place: Royal York Hotel, Toronto. Time: June 19-21, 1940.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. William Fellowes Morgan, 50 W. 50th St., New York.
Secretary: Miss Regina E. Schneider, 50 W. 50th St., New York.
Executive Director: Mrs. Eleanor Brown Merrill, 50 W. 50th St., New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Andrew Rados, 31 Lincoln Park, Newark.
Secretary: Dr. William F. McKim, 317 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. E. G. Nadeau, 122 E. Walnut St., Green Bay.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.
Place: The Gateway Inn, Land O'Lakes. Time: June 1940.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Edwin B. Goodall, 101 Bay State Rd., Boston.
Secretary-Treasurer: Dr. Trygve Gundersen, 243 Charles St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. Frederick G. Sprowl, 421 Riverside Ave., Spokane, Wash.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.
Place: Spokane, Wash. Time: June 24-27, 1940.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Clarence W. Shannon, 4th and Pike Bldg., Seattle.
Secretary-Treasurer: Dr. Purman Dorman, 1215–14th Ave., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. L. A. Shultz, 303 N. Main St., Rockford, Ill.
Secretary-Treasurer: Dr. J. J. Potter, 303 N. Main St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Don M. Howell, Alma, Mich.
Secretary-Treasurer: Dr. Louis D. Gomon, 308 Eddy Bldg., Saginaw, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. R. A. Kelly, 304 N. Main St., Mitchell, S. D.
Secretary-Treasurer: Dr. J. C. Decker, 515 Frances Bldg., Sioux City, Iowa.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Grady E. Clay, Medical Arts Bldg., Atlanta, Ga.
Secretary: Dr. John R. Hume, 921 Canal St., New Orleans.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. Dake Biddle, 123 S. Stone Ave., Tucson, Ariz.
Secretary: Dr. M. P. Spearman, 1001 First National Bank Bldg., El Paso, Texas.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. Carl Wencke, Battle Creek.
Secretary-Treasurer: Dr. A. K. Zinn, Battle Creek.
Time: Third Thursday of alternate months.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. M. Harris, Johnstown.
Secretary-Treasurer: Dr. C. Wearne Beals, 41 N. Brady St., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. Virgil Payne, Pine Bluff.
Secretary-Treasurer: Dr. Raymond C. Cook, 1005 Donaghey Bldg., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. Melville Black, 424 Metropolitan Bldg., Denver.
Secretary: Dr. John C. Long, 324 Metropolitan Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Shirley H. Baron, 309 State St., New London.
Secretary-Treasurer: Dr. S. J. Silverberg, 201 Park St., New Haven.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. Grady E. Clay, 384 Peachtree St. N. E., Atlanta.
Secretary-Treasurer: Dr. J. Mason Baird, 511 Medical Arts Bldg., Atlanta.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. Marlow W. Manion, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: Indianapolis. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. H. H. Lamb, American Bank Bldg., Davenport.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.
Place: Davenport.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. D. C. Montgomery, 301 Washington Ave., Greenville, Miss.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.
Place: St. Charles Hotel, New Orleans. Time: April 25, 1940.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. O. B. McGillicuddy, 124 W. Allegan St., Lansing.
Secretary: Dr. A. R. McKinney, 330 S. Washington Ave., Saginaw.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. Hendrie W. Grant, 330 Lowry Medical Arts Bldg., St. Paul.
Secretary-Treasurer: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. Roy Grigg, Bozeman.
Secretary: Dr. A. W. Morse, 507 Phoenix Bldg., Butte.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr. James S. Shipman, 542 Cooper St., Camden.
Secretary: Dr. Wright McMillan, 23 Passaic Ave., Passaic.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Algernon B. Reese, 73 E. 71st St., New York.
Secretary: Dr. Chester C. Cott, 333 Linwood Ave., Buffalo.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. A. G. Woodward, 100 S. James St., Goldsboro.
Secretary-Treasurer: Dr. M. R. Gibson, Professional Bldg., Raleigh.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. N. A. Youngs, 322 De Mers Ave., Grand Forks.
Secretary-Treasurer: Dr. F. L. Wicks, 516–6th St., Valley City.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
Secretary-Treasurer: Dr. R. S. Fixott, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. S. B. Fishburne, 1430 Marion St., Columbia.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. J. B. Stanford, 899 Madison Ave., Memphis.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. J. W. Ward, 2607½ Lee St., Greenville.
Secretary: Dr. Dan Brannin, Medical Arts Bldg., Dallas.
Place: Fort Worth. Time: December 1940.

Utah Ophthalmological Society

President: Dr. A. E. Callaghan, Boston Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Rowland H. Merrill, 1010 First National Bank Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Charles T. St. Clair, 418 Bland St., Bluefield, W. Va.
Secretary-Treasurer: Dr. M. H. Williams, 30½ Franklin Rd. S. W., Roanoke.

West Virginia State Medical Association, Eye, Ear, Nose and Throat Section

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. L. E. Brown, Second National Bldg., Akron, Ohio.
Secretary-Treasurer: Dr. C. R. Anderson, 106 S. Main St., Akron, Ohio.
Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. Arthur G. Fort, 478 Peachtree St. N. E., Atlanta, Ga.
Secretary: Dr. Lester A. Brown, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p m., second Wednesday of each month from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Frank B. Walsh, Wilmer Institute, Johns Hopkins Hospital, Baltimore.
Secretary: Dr. Fred M. Reese, 6 E. Eager St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to May.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. N. E. Miles, 408 Medical Arts Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. E. Clifford Place, 59 Livingston St., Brooklyn.
Secretary-Treasurer: Dr. Frank Mallon, 1135 Park Pl., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. James G. Fowler, 412 Linwood Ave., Buffalo.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. A. H. Benz, 706 Medical Arts Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Georgiana Dvorak-Theobald, 715 Lake St., Oak Park, Ill.
Secretary-Treasurer: Dr. Earle B. Fowler, 55 E. Washington St., Chicago.
Place: Medinah Michigan Avenue Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati Ophthalmic Club

Chairman: Each member, in rotation.
Secretary-Treasurer: Dr. E. R. Thomas, 819 Carew Tower, Cincinnati.
Place: Holmes Memorial Library, Cincinnati General Hospital. Time: 8:15 p. m., third Monday of each month except June, July and August.

Cleveland Ophthalmologic Club

Chairman: Dr. Albert J. Ruedemann, Cleveland Clinic, Cleveland.
Secretary: Dr. B. J. Wolpaw, 2323 Prospect Ave., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. Alexander G. Fewell, 1924 Pine St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. Harry M. Sage, 9 Buttles Ave., Columbus, Ohio.
Secretary-Treasurer: Dr. Hugh C. Thompson, 289 E. State St., Columbus, Ohio.
Place: The Neil House. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. F. K. Stroud, 416 Chaparral St., Corpus Christi, Texas.
Secretary: Dr. Arthur Padilla, 414 Medical Professional Bldg., Corpus Christi, Texas.
Time: Second Friday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Dan Brannin, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. L. E. Darrough, 4105 Live Oak St., Dallas, Tex.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. E. G. Linn, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Grace Doane, 614 Bankers Trust Bldg., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Arthur S. Hale, 1609 Eaton Tower, Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Detroit Ophthalmological Society

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. L. A. Hulsebosch, 191 Glen St., Glen Falls.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. R. A. Gough, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. Charles R. Lees, 806 Medical Arts Bldg., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Grand Rapids Eye, Ear, Nose and Throat Society

President: Dr. Dewey R. Heetderks, 405 Medical Arts Bldg., Grand Rapids, Mich.
Secretary-Treasurer: Dr. Robert G. Laird, 116 E. Fulton St., Grand Rapids, Mich.
Place: Various local hospitals. Time: Third Thursday of alternating months, September to May.

Houston Academy of Medicine, Eye, Ear, Nose and Throat Section

President: Dr. J. Charles Dickson, 1617 Medical Arts Bldg., Houston, Texas.
Secretary: Dr. William J. Snow, 708 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Otolaryngological Society

President: Dr. C. W. Rutherford, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to June.

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. E. N. Robertson, Concordia, Kan.
Secretary: Dr. John S. Knight, 1103 Grand Ave., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. Ben K. Parks, 619 Professional Bldg., Long Beach, Calif.
Secretary-Treasurer: Dr. Paul Nilsson, 211 Cherry Ave., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. John P. Lordan, 2007 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Colby Hall, 1136 W. 6th St., Los Angeles.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

LOUISVILLE EYE AND EAR SOCIETY

President: Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, Brown Bldg., Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Earle Breeding, 1801 I St. N. W., Washington.
Secretary: Dr. Elmer Shepherd, 1606–20th St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sonders, Medical Arts Bldg., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month.

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President: Dr. Herbert G. Smith, 411 E. Mason St., Milwaukee.
Secretary-Treasurer: Dr. John B. Hitz, 411 E. Mason St., Milwaukee.
Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

MONTREAL OPHTHALMOLOGICAL SOCIETY

President: Dr. L. de G. Joubert, 690 Dunlop St., Montreal, Canada.
Secretary: Dr. K. B. Johnston, 1509 Sherbrooke St. W., Montreal, Canada
Time: Second Thursday of October, December, February and April.

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Guy Maness, 119–7th Ave., Nashville, Tenn.
Secretary-Treasurer: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.
Secretary: Dr. Frederick A. Wies, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to June.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. David H. Webster, 140 E. 54th St., New York.
Secretary: Dr. Robert K. Lambert, 10 101–15th Ave., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Arthur M. Yudkin, 257 Church St., New Haven, Conn.
Secretary: Dr. Benjamin Esterman, 515 Park Ave., New York.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. J. T. Maxwell, 1140 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President. Dr. R. N. Berke, 430 Union St., Hackensack, N. J.
Secretary-Treasurer: Dr. T. A. Sanfacon, 340 Park Ave., Paterson, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

Chairman: Dr. Walter I. Lillie, 255 S. 17th St., Philadelphia.
Secretary: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. Adolph Krebs, 509 Liberty Ave., Pittsburgh.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. Rudolph Thomason, Professional Bldg., Richmond, Va.
Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Edwin S. Ingersoll, 26 S. Goodman St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.
Place: Rochester Academy of Medicine, 1441 East Ave. Time: 8 p. m., second Wednesday of each month from September to May.

St. Louis Ophthalmic Society

President: Dr. J. F. Hardesty, Missouri Theatre Bldg., St. Louis.
Secretary: Dr. Carl C. Beisbarth, 3720 Washington Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmolo-Oto-Laryngological Society

President: Dr. Oscar H. Judkins, 414 Navarro St., San Antonio, Texas.
Secretary-Treasurer: Dr. Wilfred E. Muldoon, 414 Navarro St., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Matthew Hosmer, 384 Post St., San Francisco.
Secretary: Dr. Fred Boyle, 490 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. I. Henry Smith, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Walter W. Henderson, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. Robert L. Pohl, 407 Riverside Ave., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. James F. Cahill, 428 S. Salina St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. Herbert Katz, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. S. H. Patterson, 1251–15th St., Toledo, Ohio.
Secretary: Dr. J. E. Minns, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. Ernest Sheppard, 927 Farragut Sq. N. W., Washington, D. C.
Secretary-Treasurer: Dr. E. Leonard Goodman, 1801 I St. N. W., Washington, D. C.
Place: Episcopal Eye and Ear Hospital. Time: 7:30 p. m., first Monday in November, January, March and April.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.